DISEASES OF THE BREAST

By

C D HAAGENSEN M D

*Professor of Clinical Surgery The College of Physicians
and Surgeons Columbia University
Director of Surgery The Francis Delafield Hospital
Columbia Presbyterian Medical Center*

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To my wife

ALICE MUNRO HAAGENSEN

PREFACE

In this book I have tried to present a synthesis of what I have learned during twenty five years of specialized concentration on diseases of the breast I wish to emphasize at once that this knowledge is a product of the medical environment in which I have worked at the Columbia Presbyterian Medical Center in New York The book is based not only upon my personal experience but upon all the data concerning diseases of the breast which have accumulated in our records during the forty year period 1915 to 1955

When I came to Columbia in 1931 I had already acquired from Dr Ewing and his associates at the old Memorial Hospital an abiding interest in neoplastic disease At Columbia I found the environment of a modern medical center which permitted my specialized interest particularly in diseases of the breast to evolve In these modern times when the sum of knowledge concerning even a subject of limited scope has grown so that it is beyond the grasp of any one individual I feel no need to justify specialization More than 2000 years ago the Greeks first proved the value of specialization in the sciences In modern medicine our specialization on an anatomical and disease basis merely carries this inevitable and desirable trend one step farther A basic qualification however is that the specialist have ready access to the world of medical knowledge outside his own limited sphere Otherwise he is hopelessly handicapped in dealing with the complex problems that sick patients usually present The modern medical center—a family of specialized hospitals and services with closely integrated house and attending staffs—provides this kind of environment

I should like to describe some of the basic facilities at the Columbia Presbyterian Medical Center which have made this book possible The first of these has been a Unit Record System It was established in 1915 and has been organized with great efficiency by Miss Dorothy Kurtz I am indebted to her for teaching me how to adapt the punch card method of statistical analysis to the problem of correlating the findings in our breast carcinoma cases.

In its establishment of a follow up system for surgical patients the Presbyterian Hospital was preceded only by the Massachusetts General Hospital Our follow up system was organized in 1915 by Dr James Corscaden and the late Dr Hugh Auchincloss One of the reasons why it has been so successful is that it has been a personal follow up each attending surgeon following his own ward patients just as if they were private patients I have been able to trace every one of the ward and private patients in my personal series of radical mastectomies In this

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task I have had the devoted assistance of Miss Florence Harvey, Miss Retta Pinney, and Miss Gertrude Taylor A complete follow-up of this kind is, it seems to me, a fundamental obligation for us Unless the fate of all our patients is known, their individual contributions to the knowledge of their disease—made at so great a cost—are entirely lost

Dr Arthur Purdy Stout, until his retirement three years ago the Director of our laboratory of Surgical Pathology, has contributed greatly, not only to this book, but to all the other aspects of our attack upon neoplastic disease at Columbia Trained as a surgeon as well as a pathologist, Dr Stout has been able to focus clinical as well as microscopical skill upon the special problem that tumors present He has made the frozen section method of diagnosis a dependable, and therefore an invaluable, aid to our surgeons His studies in the histogenesis of neoplasms are well known Dr Stout welcomed me into his laboratory when I first came to Columbia He has been my inspiration ever since This book is based upon the pathological material that he collected and studied over a period of forty years—1915 to 1955 We have worked together at interpreting it The book is therefore his as much as it is mine

All of us at Columbia who have worked at the special problems of neoplasia in the years gone by owe our opportunity to our beloved surgical chief, Dr Allen O Whipple I am particularly indebted to him because he took me into his department and permitted me to specialize when specialization was not popular He always supported and encouraged me in my clinical as well as my laboratory research

There are a number of other individuals who have made important contributions to this book Dr Edith Cooley, our statistician, has worked tirelessly getting out the statistical data from our case records, analyzing them, and putting them into the form in which I have presented them Mrs Grace MacQueen, with her thorough familiarity with our records, and the subject matter itself, has been a great help in the preparation of the book My wife has been my editorial mentor, correcting my manuscript with great patience, and verifying the entire bibliography

In regard to the bibliography I should point out that it is a selected and not a complete one I possess a substantially complete bibliography on diseases of the breast but it seemed wisest to select from it for inclusion in this book those items which not only contribute something but which are easily accessible to American and Western European readers

I am deeply indebted to my surgical associates Dr Joseph McDonald and Dr David Habif for help with many of the surgical aspects of this work during the past years, to Dr Stout's successor, Dr Raffaele Lattes, for continuing assistance regarding matters of pathology, to Dr John Pickren for certain pathological studies of his which I have included, to Dr Virginia Apgar for help with the special problems of anesthesia, to Dr Perry Hudson for assistance in regard to methods of hormone therapy, and to Dr Maurice Lenz, until recently Director of Radiotherapy at the Francis Delafield Hospital, and to his successor, Dr Ruth Guttmann, for help in all matters pertaining to radiotherapy

For many years Dr Stout, Dr Lenz, Dr John Hanford, and I conducted a Neoplasm Clinic in the Presbyterian Hospital We learned to understand and

value each other's point of view and to integrate our surgical and radiotherapeutic attack upon breast carcinoma Dr Lenz taught us what intensive highly fractionated irradiation administered with meticulous care and great patience can accomplish In his hands radiotherapy is a precise weapon and its use is based upon principles which the surgeon can understand The spirit of cooperation between surgeons and radiotherapeutists both being guided by the facts revealed by pathology continues in our special cancer hospital the Francis Delafield Hospital recently added to the Columbia Presbyterian Medical Center The exceptional facilities for clinical cancer research provided in the Francis Delafield Hospital have made possible a number of recent studies which I have reported in this book

Others who have helped with the preparation of the book have been Robert Demarest and Leon Schlossberg who made the drawings Lewis Koster who together with the late Walter O'Neil made the photographs Anton Samuel research technician and the staff of the library of the College of Physicians and Surgeons The highly skilled staff of W. B. Saunders Company have made the technical aspect of the preparation of the book easy for me

C. D. Haagensen

The Columbia Presbyterian Medical Center
New York

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CHAPTER 1

ANATOMY OF THE MAMMARY GLAND

The mammary glands are a distinguishing feature of the zoological class which has been named after them—the mammals The number of pairs of breasts varies greatly among different species of mammals, but has a general relationship to the number of young in each litter For instance the rodents have six or seven pairs of breasts and the lion but two The anthropoid apes and man have but a single pair The number of mammary glands has no relationship to the tendency of carcinoma to develop in them for the disease is frequent in the mouse in the dog, and in man but is rare or unknown in other species

Anomalous Structures

The single pair of pectoral breasts with which human beings are provided is occasionally augmented by anomalous breasts or nipples situated along a line from the axilla to the groin corresponding to the nipple line in lower species of mammals and to the embryonal mammary line The incidence of such supernumerary mammary glands and nipples has been estimated at 1 per cent (Speert) The majority of these anomalous structures are situated below the normal breasts

The anomalous structures may consist only of a pigmented area representing a rudimentary accessory areola, or of a supernumerary nipple without an areola or of a complete nipple and areola. The extra nipple may have no connection with mammary tissue or it may connect with the duct system of the normal breast and function during lactation These supernumerary nipples are often situated in or near the areola of the normal breast. Complete supernumerary breasts with a well developed parenchyma and with normal physiological function are occasionally encountered

Figure 1 shows a girl aged 15 otherwise normal with a functioning supernumerary nipple about 10 cm below the inframammary fold on the right side and a supernumerary breast, complete with its own nipple just below her normal left breast. This accessory left breast enlarged premenstrually Both the right sided extra nipple and the left sided supernumerary breast were excised (service of Dr J P Webster)

Figure 2 shows a woman, aged 35 with a well developed supernumerary breast in the right axilla. She had noted its presence since she was 18 years old During each of her three pregnancies it had enlarged, and during lactation it had secreted milk through the small protuberance in its center resembling a

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CHAPTER 1

ANATOMY OF THE MAMMARY GLAND

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Figure 2 shows a woman aged 35 with a well developed supernumerary breast in the right axilla She had noted its presence since she was 18 years old During each of her three pregnancies it had enlarged and during lactation it had secreted milk through the small protuberance in its center resembling a

small nipple There was a similar but much smaller supernumerary breast which did not possesss a nipple in the left axilla

Because the large right axillary breast bothered her, the patient wished it excised This was done, and microscopical study showed abundant breast tissue with some cystic change, and a nipple of normal structure

Form

Nulliparous breasts are conical but after lactation they usually become flattened and more pendulous There is a great variation in their form and size



Fig 1 Supernumerary mammary development Right supernumerary nipple, left supernumerary breast

Obesity plays a part, for excess fat has a tendency to accumulate in the breasts

It is important to point out that the two breasts are often unequal in size, although perfectly symmetrical in contour The clinician alert for inequalities produced by neoplasms must not confuse differences in size which are developmental in origin, with those due to pathologic changes

These developmental differences in the breasts may sometimes be marked The following case illustrates the phenomenon

C. G came to the Presbyterian Hospital at the age of 13 complaining that her breasts were unequal in size Menstruation had begun at the age of 11 and her breasts began to develop at about the same time A year later it was noted that the left breast was smaller than the right Both breasts slowly enlarged but the left continued to be about one half the size of the right This discrepancy still persisted when the patient was last seen at the age of 18 (Fig 3) At this time the right breast was entirely normal but the left one continued comparatively undeveloped There was no associated endocrine abnormality



Fig 2. Bilateral supernumerary axillary breast The right-sided one is larger and has a nipple

In old age the breasts often atrophy markedly They not only decrease in size but become very loose in texture This change makes the detection of tumors easier

Extent

The protuberant breast extends from the second or third rib to the sixth or seventh costal cartilage and from near the edge of the sternum to the anterior axillary line The actual extent of the mammary tissue is considerably greater however It is spread out as a thin layer which often reaches the clavicle above the midline medially and the edge of the latissimus dorsi muscle laterally This

is a fact of importance to the surgeon attacking carcinoma of the breast, who should extend his dissection far enough at least to remove all of the breast This wide superficial extent of the breast tissue is evident in certain cases of acute postpartum engorgement of the breasts We have also seen proof of it in studying microscopical sections from subcutaneous tissues from areas beyond the protuberant breast

The upper outer sector of the breast is thicker than the remainder of the breast The fact that this sector contains a greater bulk of mammary tissue than

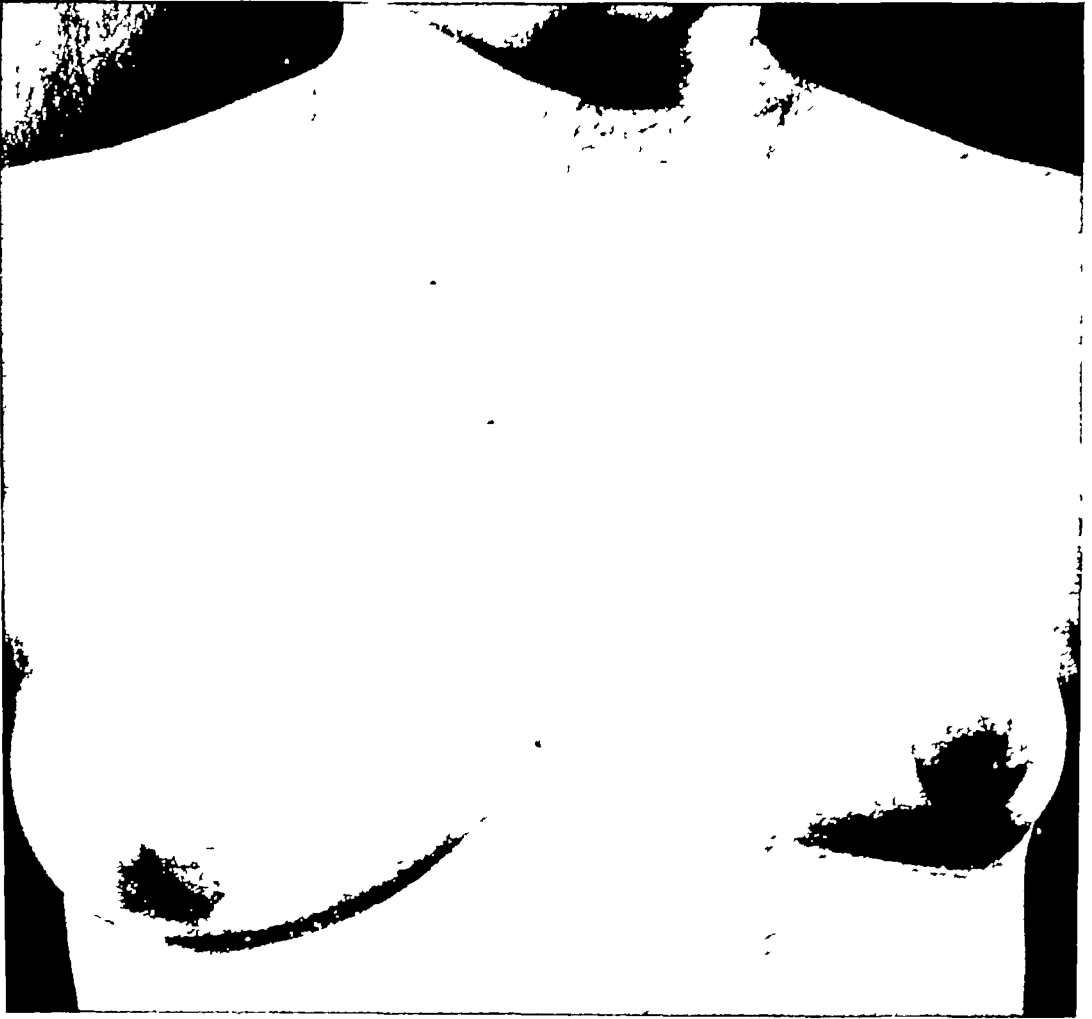


Fig 3 Underdevelopment of left breast

other sectors may account for the fact that both benign and malignant tumors are more frequent in it

The breast also extends into the axilla to a variable degree This axillary projection or "tail" is sometimes so large that it forms a visible axillary mass which enlarges premenstrually and during lactation Roux has recently described actual secretion of milk from axillary breast tissue Such well developed axillary projections of the mammary gland are commonly mistaken for axillary lipomas or enlarged axillary lymph nodes Carcinoma may develop in the axillary projection and confuse the diagnostician

Figure 4 shows a prominent left axillary projection of the mammary gland in a single woman aged 32 She had noted the left *axillary tumor for only one* month It was soft and measured about 5 cm in diameter Its lower pole merged with the upper outer part of the left breast and there was no supernumerary nipple or areola to suggest that the axillary mass was a separate supernumerary

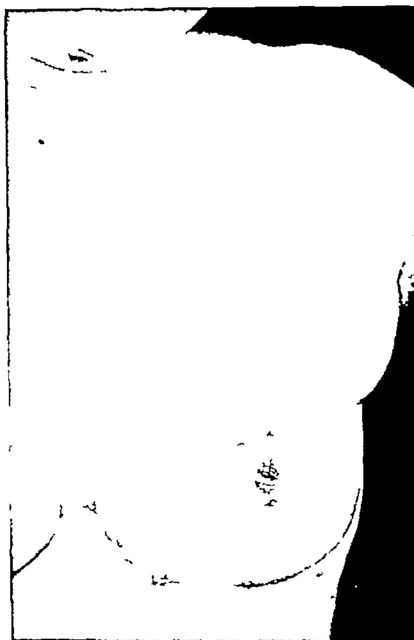


Fig 4 Axillary projection of the left mammary gland.

mammary gland There was a homologous but considerably smaller axillary projection on the right side The left breast was considerably smaller than the right

The left axillary mass was excised and proved to be *mammary tissue* Microscopical study showed some of the ducts to be dilated, and papillary epithelial proliferations in others

Fig 5 Numerous and large lobules in the breast of a woman aged 22

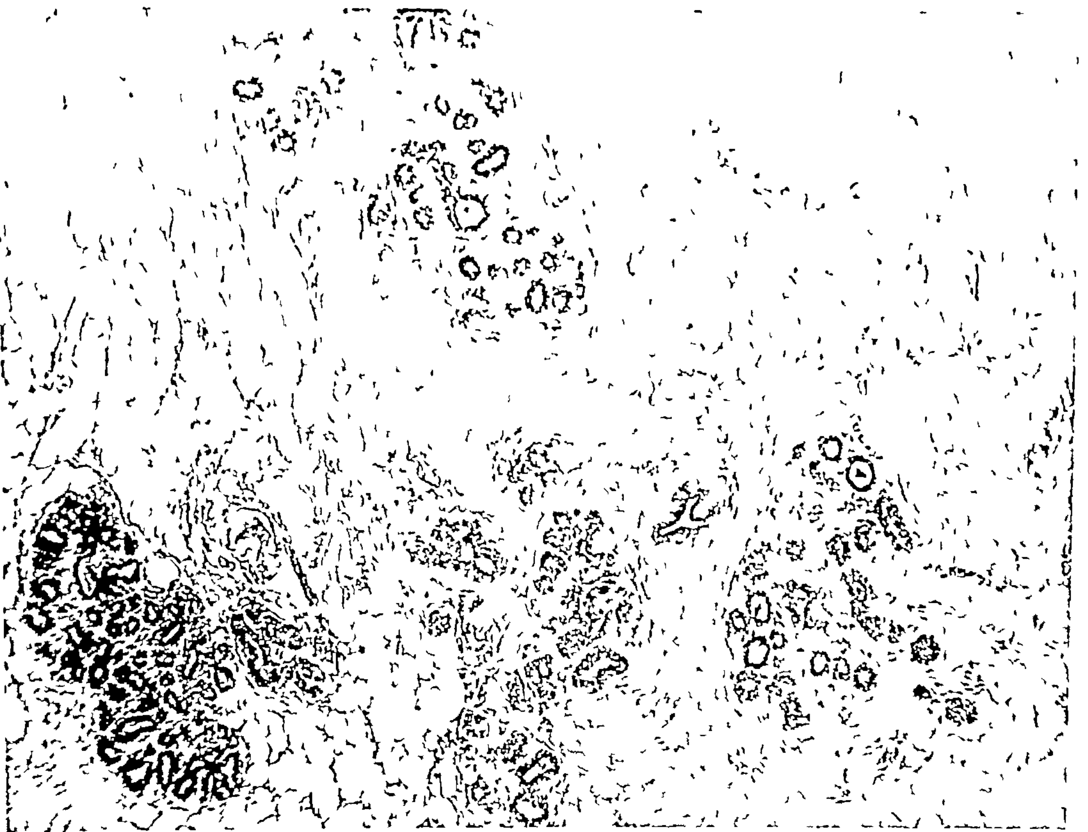


Fig. 6. Variation in lobule size in the breast of a woman aged 22

Structure

In addition to its fascial elements the breast consists of a varying amount of fat blood vessels nerves and lymphatics and of course, its epithelial parenchyma of acini and ducts The connective tissue and epithelial elements are so inextricably intermingled that the surgeon can find no planes of dissection within the gland itself He must always cut attempts to use blunt dissection are futile

The epithelial parenchyma is made up of from fifteen to twenty *lobes* each emptying into a separate excretory duct terminating in the nipple The lobes in their turn are divided into a multitude of lobules or gland fields each made up of from ten to a hundred or more acini grouped around a collecting duct.

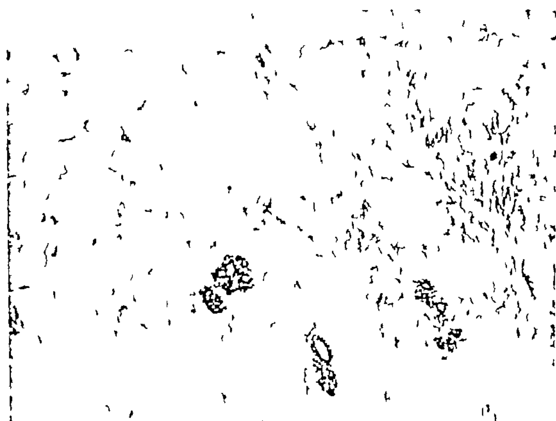


Fig 7 Atrophic lobules in the breast of a woman aged 61

The *lobule* is thus the basic structural unit of the mammary gland and as such deserves close study The number and size of the lobules vary exceedingly and not always according to the developmental stage of the subject. In general they are largest and most numerous during young womanhood (Figs 5 and 6) After the menopause the lobules often decrease in size so that each comes to consist of only three or four acini (Fig 7) Sometimes only the collecting duct remains to mark the site of a lobule It is not unusual however to see numerous and well preserved lobules persisting in women of advanced age, or to find them small and few in young women

The *acini* in the resting mammary gland are lined by a single layer of cuboidal or cylindrical epithelial cells (Fig 8) Occasional additional cells around the base of the acinus suggest a second layer of epithelial cells These basal cells are the so-called myoepithelial cells

Fig 8 Normal epithelium of mammary gland acini

Fig 9 Collagenous sheath of mammary gland acini Laidlaw silver stain

Each acinus is enveloped by a delicate but well defined collagen sheath or basement membrane, which is best shown by a silver stain (Fig 9) This sheath is prolonged to invest the collecting duct. The lobule as a whole has a somewhat thicker collagen envelope enclosing it

The *myoepithelial cells* of the breast have a special interest for the student of mammary neoplasms because they take part in certain benign yet cancer like proliferations which can only be properly interpreted in the light of the normal characteristics of the myoepithelial cells (Hamperl Kuzma) These cells are best seen in the smaller ducts They lie directly upon the basement membrane, beneath the inner layer of lining epithelium They are elongated in shape with dense oval nuclei and delicate cytoplasmic fibrils closely resembling smooth muscle cells (Fig 10) They have a spiral arrangement around the ducts, as



Fig. 10 Myoepithelial cells as seen in a transverse section through the wall of a small duct.

shown in Figure 11 in which the duct wall has been sectioned eccentrically in its long axis Although their exact function remains unproved the myoepithelial cells provide a muscular mechanism which may serve to narrow and empty the ducts.

The details of the structure and arrangement of the myoepithelial cells can be seen only after proper fixation and staining Masson s trichrome stain is the best means for demonstrating them The myoepithelial layer of cells thins out as it approaches the acini, and is difficult or impossible to trace in normal acini It is also lost to view in the larger collecting ducts In these main collecting ducts there are two well defined layers of cylindrical epithelial cells, as shown in Figure 12

As the main collecting ducts approach the surface of the nipple they dilate and a sac like milk sinus is formed (Fig 13) This sinus is lined by stratified

Fig 11 The spiral arrangement of the myoepithelial cells in the wall of a small duct cut eccentrically in its long axis



Fig 12 Main collecting duct of mammary gland with two layers of epithelium

squamous epithelium (Fig 14) In the resting mammary gland it is filled with epithelial debris

The *nipple* and *areola* contain several tissues which are of special interest in that they may give origin to neoplasms Both the subareolar area and the nipple

Fig 13 Vertical section through nipple showing milk sinus in terminal portion of collecting ducts.

Fig 14 Stratified squamous epithelium of milk sinus

Fig 11 The spiral arrangement of the myoepithelial cells in the wall of a small duct cut eccentrically in its long axis

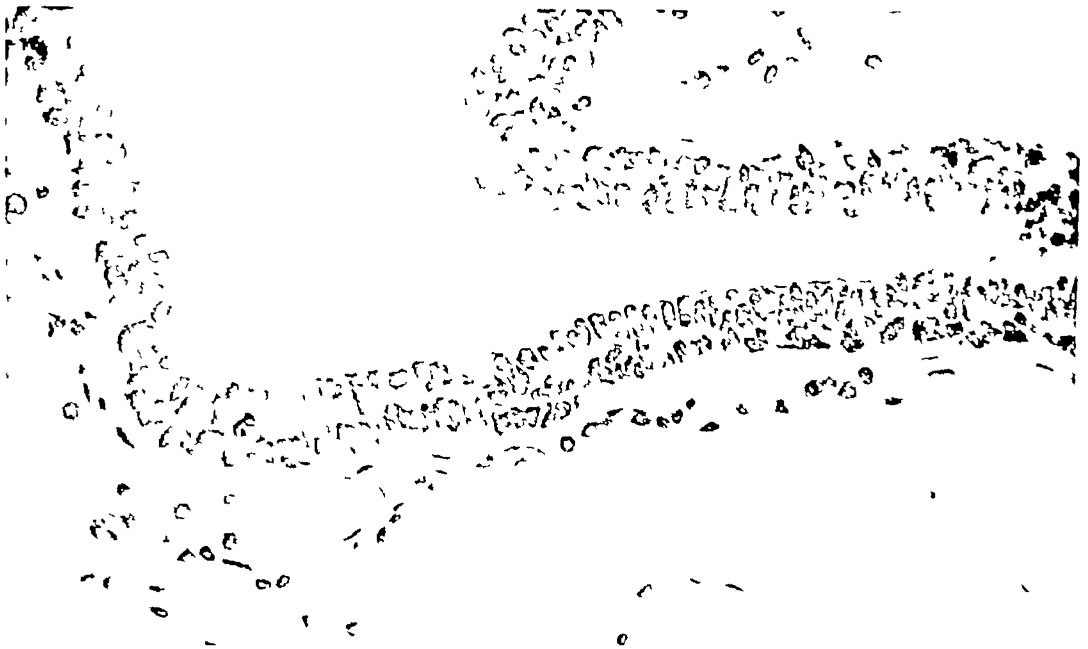


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Fig 13 Vertical section through nipple showing milk sinus in terminal portion of collecting ducts

Fig 14 Stratified squamous epithelium of milk sinus.

contain much smooth muscle In the subareolar area its fibers are arranged in concentric rings, as well as radially They insert into the base of the derma, and function to contract the areola and to compress the base of the nipple

The bulk of the nipple is made up of smooth muscle fibers arranged both circularly and longitudinally (Fig 13) When they contract they make the nipple erect, smaller, and firmer, and empty the ducts and milk sinuses

The areolar epithelium contains some small hairs and numerous glands These latter are of three types sweat glands, sebaceous glands, and accessory mammary glands The sebaceous glands are large and superficially situated, and project as a series of small nodules from the surface of the areola They have been called *Morgagni's tubercles* During pregnancy these tubercles enlarge strikingly and the obstetrician designates them as Montgomery's tubercles

There are also, in the areola, in some individuals, a small number of deeply situated accessory mammary glands Their structure is the same as that of the mammary gland proper Their miniature ducts open into small sinuses in the

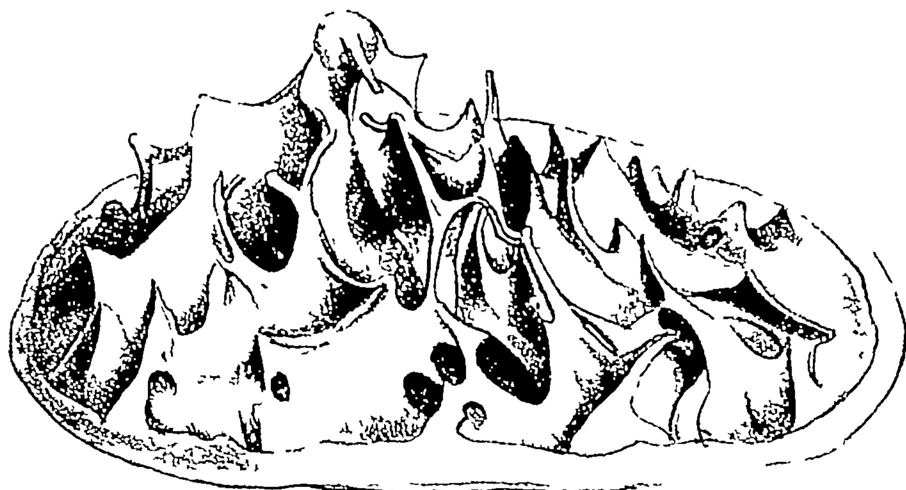


Fig 15 Cooper's ligaments of the breast (From The Anatomy and Diseases of the Breast by Sir Astley Cooper, Lea & Febiger, Philadelphia, 1845)

areolar epithelium The fact that they are indeed mammary glands is proved by secretion of milk from them during lactation

The epithelium of the nipple is elevated in high papillary folds It contains neither hair follicles nor sweat glands but has a great number of sebaceous glands which are often grouped around the openings of the milk sinuses

Fascial Relationships of the Mammary Gland

Since the mammary gland is a modified cutaneous gland, an appendage of the skin, so to speak, it is enclosed between the superficial and deep layers of the superficial fascia The superficial layer of this fascia is a very delicate but definite structure which will be seen only by the surgeon who looks sharply for it and who keeps the operative field dry enough to permit its identification The anatomist in his dissecting room is usually unable to identify it This fascial layer is important to the surgeon because it provides him with a good guide if he wishes to dissect up skin flaps through a relatively avascular plane and not include on them any mammary tissue This is accomplished by dissecting just

outside of the superficial layer of the superficial fascia and preferably by beginning at the caudad end of the wound where the fascia is better developed. It becomes more and more delicate as the clavicle is approached In thin individuals dissection through this plane leaves only 2 or 3 mm of fat and areola tissue on the skin flaps in obese individuals several additional millimeters of fat may be found superficial to the fascia Dissection in this plane passes deep to the network of small blood vessels in the corium but is superficial to the larger vessels and lymphatics that lie beneath the superficial layer of the superficial fascia.

Cooper s ligaments which Astley Cooper described and pictured so well a century ago are peripheral tooth like projections of the breast tissue in fibrous processes which reach and fuse with the superficial layer of the superficial fascia By these processes, Cooper wrote the breast is slung upon the forepart of the

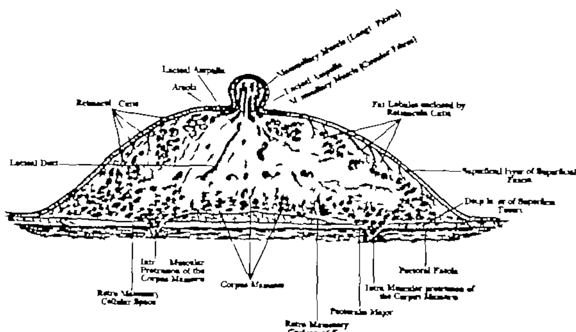


Fig 16 The fascial relationships of the breast shown diagrammatically (From Cancer of the Breast Clinically Considered by Cecil H Leaf Constable & Company Ltd)

chest, for they form a movable but very firm connection with the skin so that the breast has sufficient motion Figure 15 reproduces Cooper's original drawing of his dissection of the suspensory ligaments These fibrous processes are important clinically because the intimate connection between the breast and the skin which they provide results in skin retraction in carcinoma and in certain other breast lesions accompanied by fibrosis

Stiles showed by means of his nitric acid method of fixation, which differentiates parenchyma and stroma in gross specimens that the parenchyma of the breast is prolonged peripherally in these Cooper ligaments so that it reaches almost up to the corium Stiles quite properly concluded that the surgeon who intends to excise the whole of such a gland (the breast) must either sacrifice a large amount of skin or keep so close to it in dissecting it off the mamma as to run some risk of sloughing

Between the deep layer of the superficial fascia on the posterior aspect of the

breast, and the deep fascia covering the pectoralis major and other muscles of the chest wall, there is a well defined space, sometimes called the retromammary bursa It contains loose areolar tissue which allows for a degree of mobility of the breast over the chest wall The surgeon excising a portion of the mammary gland knows at once that he has reached the back of the breast when his knife falls into this loose areolar tissue

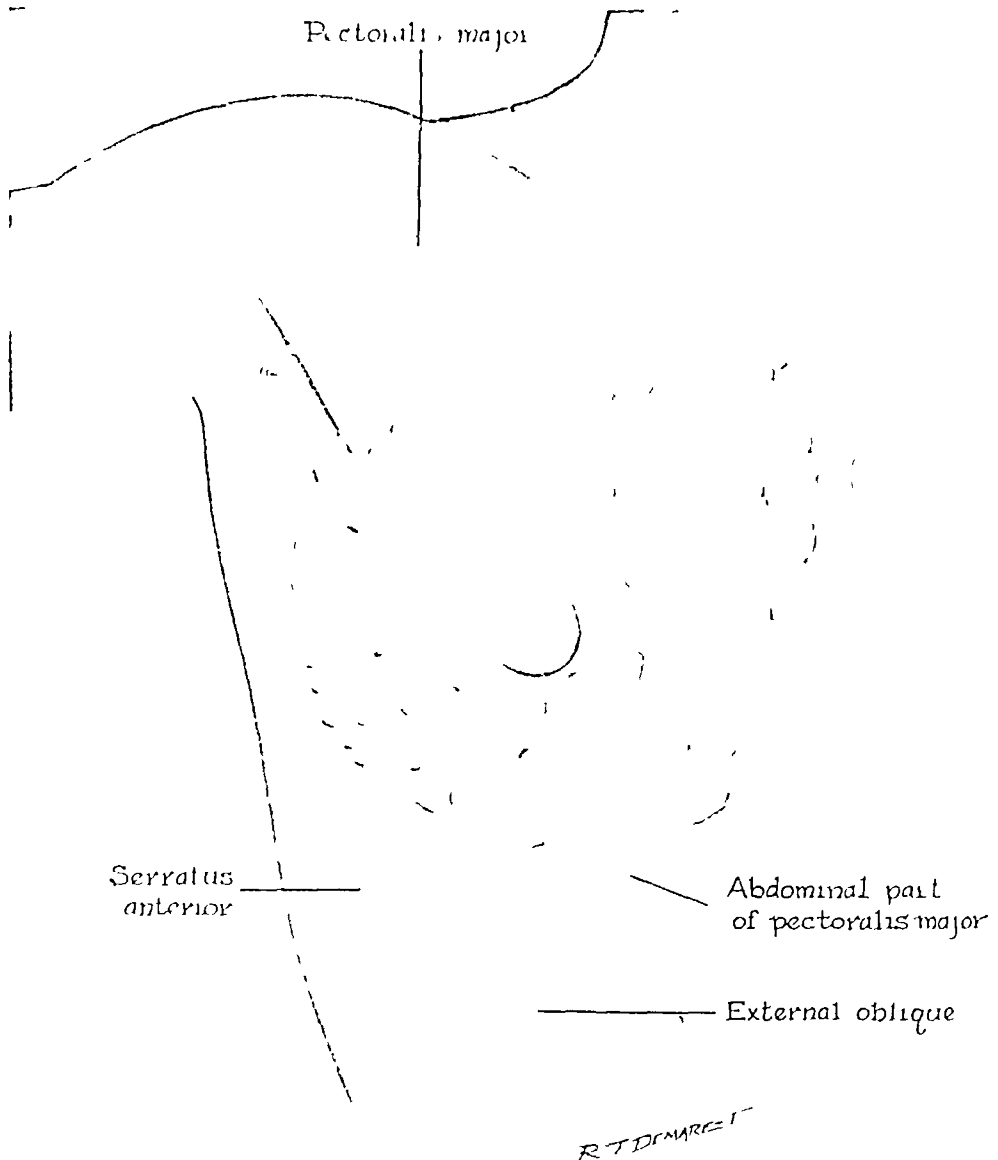


Fig 17 A dissection of the breast to show its anatomical relationships

Projections of the deep layer of the superficial fascia cross the retromammary space and fuse with the deep or pectoral fascia These form the posterior suspensory ligaments of the breast Stiles showed that small islands of breast parenchyma accompany these fibrous processes which are attached to the pectoral fascia In order to excise all mammary tissue the pectoral fascia must therefore be carefully dissected from the muscle Since deep projections of mammary parenchyma sometimes dip in-between the muscle bundles of the pectoralis muscle, it may even be desirable to remove a thin layer of muscle

These fascial relationships are well shown in Leaf's drawing (Fig 16) which we have reproduced with his terminology

Although it is customary to speak of the breast as lying upon the pectoral fascia only a part of the gland, perhaps one half in fact overlies the deep fascia of the pectoralis major The remainder of the breast lies upon the other muscles clothing the chest wall lateral and caudad to the axillary border of the pectoralis major When the arm is extended to shoulder level the edge of the pectoralis major is elevated exposing the fourth serration of the serratus magnus muscle The breast then overlies the fourth fifth sixth and seventh (in part) serrations of this muscle More medially it overlies the interdigitations of the external oblique with the serratus Near the midline a small portion of the breast overlies the rectus abdominis All of these muscles are of course covered by the same deep fascia which blends them together Figure 17 shows the fascial relationships

The Axillary Fasciae

The fasciae of the axilla are of great practical importance to the surgeon and he must know them thoroughly

The deep layer of fascia which everywhere covers the muscle plane has a complex arrangement in the pectoral and axillary region Here it not only forms septa which enclose and separate the two pectoral muscles but in so doing it spans the axillary space and forms a bridge, so to speak which stretches across the axilla from the deltoid muscle and the clavicle above to the chest wall muscles below It has two strata a superficial one called the *pectoral fascia* which invests the pectoralis major muscle and a deeper one the *costocoracoid fascia* which invests the pectoralis minor muscle

The *pectoral fascia* covers the external surface of the pectoralis major and is so intimately connected with its fibers that it is difficult to dissect it cleanly away from the muscle as the surgeon sometimes needs to do Medially the pectoral fascia is continuous across the midline with the pectoral fascia of the opposite side Laterally it turns around the lateral border of the pectoralis major to cover its deep surface Cephalad, it is continuous with the fascia of the deltoid and the fascia over the clavicle

The *costocoracoid* fascia is a deeper and thicker layer of fascia spanning the axilla, revealed when the pectoralis major muscle is turned back as in Eisler s drawing (Fig 18) It has a special importance for the surgeon attempting to dissect the axilla because it guards the nerves, vessels, and lymphatics that traverse the axilla As Leaf said this fascia gives coherence to the fat and lymph nodes of the axilla and makes their removal in one piece together with all of the fascia, easier than would otherwise be the case I have chosen to use the older English name *costocoracoid* fascia because it is the shortest and most truly descriptive term The German anatomists call it the deep pectoral fascia The French (Richet) call it the clavi-coraco-axillary aponeurosis and some American anatomists prefer the term clavipectoral fascia Figure 19 shows these axillary fascial relationships in diagrammatic form as seen in a sagittal section through the pectoral region

The portion of the costocoracoid fascia stretching across the inner portion

of the axilla between the clavicle and the medial border of the pectoralis minor is irregularly four-sided It contains an imperfectly rounded opening reminiscent of the fossa ovalis of the thigh, through which pass the cephalic vein, the thoraco-acromial vessels, and anterior thoracic nerves The crescentic medial edge of this opening is formed by a particularly thick and sometimes almost tendinous sheet of fascia which extends from the clavicle across the first intercostal space, to the second rib The surgeon who wishes to expose the apex of the axilla must sever the attachment of this fascia to the clavicle, the adjacent portion of the

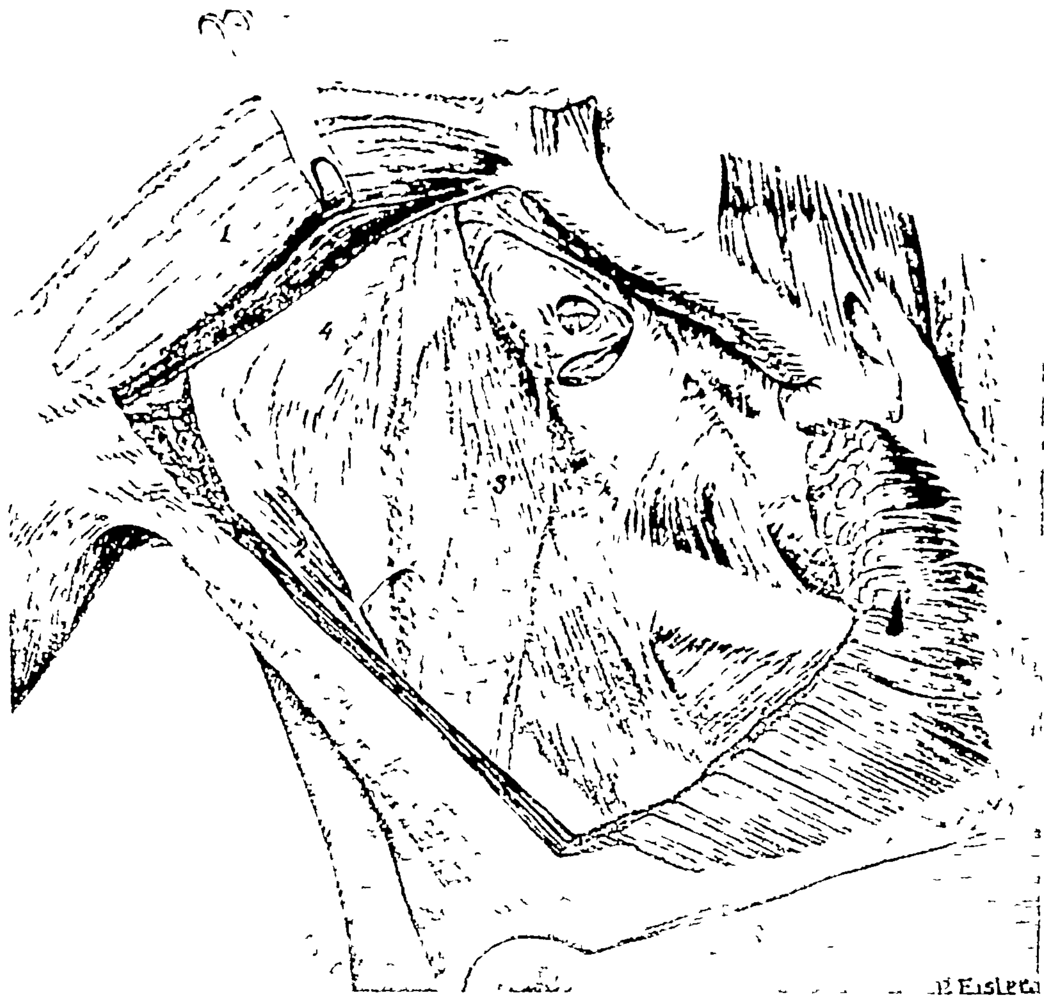


Fig 18 The costocoracoid fascia as shown after the pectoralis major has been to a large extent removed *1*, deltoid, *2*, pectoralis major, *3*, pectoralis minor, *4*, coracobrachialis (From Handbuch der Anatomie des Menschen, Paul Eisler, Jena, Gustav Fischer, 1912)

first rib, and the deep fascia over the first intercostal space This step reveals the axillary vein passing beneath the subclavius muscle, and parallel and just caudad to the vein, the collecting lymphatic trunks lying in areolar tissue and fat and also disappearing beneath the subclavius muscle

The portion of the costocoracoid fascia stretching across the outer half of the axilla from the lateral edge of the pectoralis minor muscle to the coracobrachialis muscle is triangular in shape At its base laterally it fuses with the so-called axillary fascia which forms the hollow of the axilla This portion of the

fascia is sometimes called appropriately enough the coraco axillary fascia or the suspensory ligament of the axilla From its apex at the coracoid process band like thickenings in the fascia stream laterally and caudad reinforcing the fascia as it overlies the nerves and vessels of the lateral half of the axilla The density of these reinforcing bands comes to the surgeon s attention as he severs this fascia cephalad and parallel to the axillary vein in the first step in axillary dissection

The Blood Supply of the Breast

Arteries The chief supply of the breast is from the *perforating branches of the internal mammary artery* The first second third and fourth perforating branches

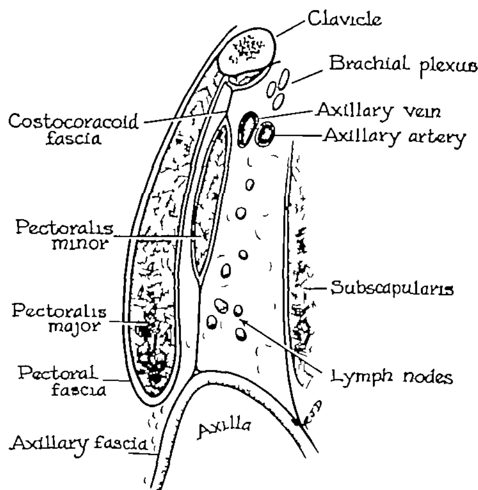


Fig 19 The fasciae of the axilla as seen in a sagittal section

perforate the chest wall near the sternal edge in the corresponding interspaces and traverse the pectoralis major muscle to reach the mammary gland along its medial edge The first perforating artery and its accompanying vein or veins usually emerge from the intercostal muscle plane near the caudad edge of the first interspace at the sternal border and are closely applied to the surface of the second costal cartilage as they arch downward across it to enter the pectoral muscle The second perforating artery is usually seen to emerge from the inter costal plane near the cephalad edge of the second interspace at the lower edge of the second costal cartilage Thus the two largest vessels supplying the breast are encountered by the surgeon just above and just below the second costal


1 2 3 4 5 6 7 8 9 10
11 12 13 14 15 16 17 18 19 20
21 22 23 24 25 26 27 28 29 30
31 32 33 34 35 36 37 38 39 40
41 42 43 44 45 46 47 48 49 50
51 52 53 54 55 56 57 58 59 60
61 62 63 64 65 66 67 68 69 70
71 72 73 74 75 76 77 78 79 80

Fig. 20 The Anatomy of the Axilla. (Pernkopf Vol 1 Part 1 Table 20 Fig. 36)

KEY TO DISSECTION OF AXILLA

1 Long head of the biceps muscle
2. Cephalic vein
3 Short head of the biceps muscle
4 Deltoid muscle
5 Ulnar nerve
6. Median nerve
7 Brachial artery
8 Coracobrachialis muscle
9 Radial nerve
10. Pectoralis major muscle
11 Brachial vein
12. Posterior humeral circumflex artery
13 Anterior humeral circumflex artery
14 Common head of the coracobrachialis and the short head *of the biceps muscles*
15 Cephalic vein
16 Anterior thoracic nerve and pectoral branch of thoraco-acromial artery
17 Musculocutaneous nerve
18 Pectoralis minor muscle
19 Deltoid muscle
20. *Subscapular nerves*
21 Acromial end of the clavicle
22. Acromial branch of thoraco-acromial artery
23 Thoraco-acromial artery
24 Coracoid process
25 Coracoclavicular fascia
26. Suprascapular artery vein, and nerve
27 *Posterior cord of* brachial plexus
28. Medial anterior thoracic nerve, and a branch of the axillary artery to the pectoralis minor
29 Lateral cord of the brachial plexus
30 Terminal portion of the cephalic vein
31 Axillary artery
32. Subclavius muscle
33 Anterior thoracic nerves
34 Subclavicular group of axillary lymph nodes
35 Clavicular branch of thoraco-acromial artery
36 Axillary vein and subclavicular lymphatic trunk
37 Tendinous origin of the serratus anterior muscle from the first rib
38 Sternoclavicular joint
39 Costoclavicular ligament
40. Branch of the first intercostal nerve
41 Highest thoracic artery
42. Cartilage of first rib
43 Internal intercostal muscle (first intercostal space)
44 External intercostal muscle (first intercostal space)
45 Pectoralis major muscle (cut at its origin)
46 Sternum (manubrium)
47 Perforating vessels in first interspace
48 Medial cord of branchial plexus
49 Cartilage of second rib
50. Origin of serratus anterior muscle from second rib
51 Thoracodorsal nerve and artery
52. The pectoralis minor muscle reflected to show branches of the thoraco-acromial artery and the artery to the pectoralis minor and branches of the anterior thoracic nerves, entering its deep surface
53 Lateral thoracic artery
54 Intercostobrachial nerve (lateral cutaneous branch of the second intercostal nerve)
55 Third rib
56 Central group of axillary lymph nodes
57 Origin of serratus anterior muscle from third rib
58 Long thoracic nerve
59 External intercostal muscle (third intercostal space)
60 Lateral cutaneous branch of the third inter costal nerve
61 External mammary group of axillary lymph nodes
62. Thoracodorsal vein
63 Costoaxillary vein
64 Origin of serratus anterior muscle from fourth rib
65 Lateral cutaneous branch of the fourth inter costal nerve
66 Long thoracic nerve
67 Insertion of serratus anterior muscle on inferior angle of scapula
68 Scapular group of axillary lymph nodes
69 Thoracodorsal nerve and artery
70 Axillary vein group of axillary lymph nodes
71 Teres major muscle
72. Subscapularis major muscle
73 Scapular circumflex artery and vein, and branch of subscapular nerve to teres major
74 Medial brachial cutaneous nerve (severed)
75 Lateral root of the medial nerve
76 Medial root of the medial nerve
77 Latissimus dorsi muscle
78 Intercostobrachial nerve
79 Medial brachial cutaneous nerve
80 Basilic vein and medial antibrachial cutaneous nerve

cartilage The lower perforators emerge at varying levels in their respective interspaces

In the upper interspaces there is a series of much smaller perforating vessels which emerge from the intercostal muscle plane 2 or 3 cm lateral to and parallel with the main perforators These secondary perforators are large enough to justify the surgeon's taking care to identify and clamp and cut them after the main perforations have been clamped and cut

Several branches of the axillary artery also share in providing blood for the breast (Fig 20) The smallest and highest of these, *the highest thoracic artery*, is a variable and inconsequential vessel which crosses from the first part of the axillary artery to the chest wall above the upper border of the pectoralis minor muscle

The *pectoral branch of the thoraco-acromial artery* descends between the pectoralis minor and major muscles It is the chief blood supply of the latter muscle After traversing the pectoralis major, some of its branches reach the deep surface of the mammary gland

A small artery, the *artery to the pectoralis minor*, arises from the second part of the axillary artery from 1 or 2 cm lateral to the origin of the thoraco-acromial trunk, or as a branch of the thoraco-acromial trunk, and crosses the axillary vein, closely applied to its surface as it runs caudad to reach the deep surface of the pectoralis minor The importance of this very small artery to the surgeon is out of all proportion to its size, for as we will point out in our description of the dissection of the axilla, cutting it and the medial anterior thoracic nerve which accompanies it, gives access to the axillary vein

The *lateral thoracic artery* arises from the second part of the axillary artery, or as a branch of the thoraco-acromial or subscapular arteries Emerging from beneath the axillary vein it crosses the axilla to the chest wall and the free outer edge of the pectoralis major to supply the lateral portion of the breast It has been called the external mammary artery It varies in size, and is not infrequently absent

The *subscapular artery* is the largest branch of the axillary artery, arising from its third portion opposite the outer border of the subscapularis muscle The subscapular gives off the scapular circumflex artery soon after it arises, and in its continuation across the surface of the subscapularis muscle to the lateral chest wall it is called the *thoracodorsal artery* It supplies the latissimus dorsi muscle and sends several large branches to the serratus magnus Difficulty in controlling bleeding from these arterial branches and their accompanying veins during radical mastectomy has given the name "the bloody angle" to this region The thoracodorsal artery is not an important supply for the breast, but in its course it is intimately associated with the central and scapular groups of lymph nodes which so often contain metastases from breast carcinoma, and the manner in which the surgeon deals with it in his axillary dissection is therefore very important

Veins The venous route is important to students of breast carcinoma not only because metastasis frequently occurs through veins, but also because veins are a key to the lymphatic pathways which in general follow the course of the veins

The superficial subcutaneous veins over the breast lie just below the super-

ficial layer of the superficial fascia and are large enough and close enough to the skin surface to be shown well by photographs taken in infrared light Massopust and Gardner have made extensive photographic studies of this kind and have classified the anatomical patterns formed by these veins into two main types In the transverse type the veins converge toward the sternal edge and then turn deeply to join the perforating vessels that pierce the chest wall and empty into the internal mammary veins In the longitudinal type of pattern the veins converge toward the suprasternal notch and empty into the superficial veins of

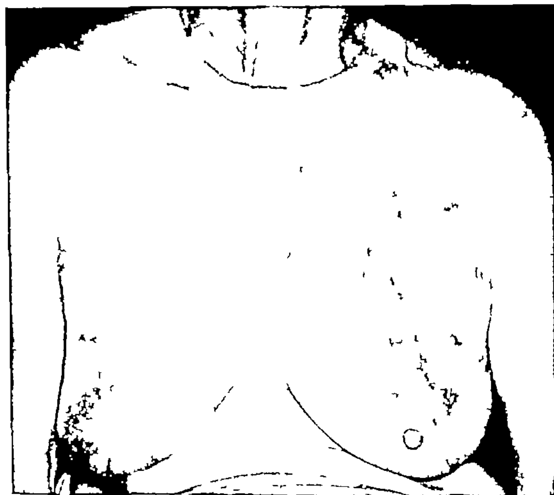


Fig 21 Superficial veins of the anterior chest wall as shown in infrared photograph. Transverse type of pattern

the lower neck that drain into the anterior jugulars Infrared photographs from our own patients illustrate these two types of patterns (Figs 21 and 22) Infrared photographs show that these superficial veins anastomose across the midline of the anterior chest wall in many patients

Infrared photographs also demonstrate nicely the circumareolar veins which are a relatively constant anatomical finding, and which surgeons who use circum areolar incisions know well

The superficial veins over the breast are often dilated over an area of the breast that contains disease and the dilatation is sometimes marked enough to be recognized by inspection in ordinary light. Tumors whether malignant or

cartilage The lower perforators emerge at varying levels in their respective interspaces

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The axillary vein itself shows great variation The junction of the basilic and brachial veins to form the axillary vein may take place at any point from the outer edge of the teres major up to the clavicle When this junction occurs high up the axillary vein is in effect double Care must be exercised not to mistake in such cases the main venous trunk from the arm for a large branch of the axillary vein coming from the lateral chest wall When in the course of an axillary dissection tension upon the specimen in a caudad direction bows the axillary vein downwards its relationships may be distorted Normally it lies medial (caudad when the arm is abducted as in an axillary dissection) to the axillary artery overlapping it so thoroughly that the artery is not seen at all during the dissection

A phenomenon which sometimes confuses the surgeon during his dissection of the axillary vein is the marked contractility of its lateral portion When the vein is first exposed it has a large caliber throughout its whole extent although tapering somewhat toward the arm Dissection of the medial portion of the vein changes its caliber very little, but dissection of the lateral half produces such sharp contraction of that portion of the vein that the surgeon may momentarily doubt that he is still dealing with the axillary trunk

The venous pathway from the breast through the axillary vein leads of course directly to the pulmonary capillary network and provides a second route to the lungs for carcinoma emboli

3 The third, and one of the most important routes of venous drainage from the breast is directed posteriorly through the *intercostal veins* These veins communicate with the vertebral veins and finally empty into the azygos vein This route through the intercostal and azygos veins leads to the superior vena cava and to the lungs It constitutes a third pathway by which carcinoma emboli produce pulmonary metastases

These three venous routes for metastases from breast carcinoma to the capillary network of the lungs are shown especially in Figure 23

The vertebral system of veins provides an entirely different route by which metastases reach the bones directly without going through the caval veins and through the lungs

The vertebral veins constitute a separate vertical system of veins, paralleling the caval system They drain blood from the vertebral column adjacent muscles and spinal cord They form intricate venous plexuses both inside and outside the vertebral canal extending along its entire length The so-called basivertebral veins form wide tortuous channels within the vertebral bodies similar to those in the diploë of the cranial bones, and empty into the anterior external vertebral plexus The vertebral plexuses communicate at each vertebral segment with the intercostal veins Figure 24 shows this communication as pictured in Gray s Anatomy

Batson has proved with injection experiments in cadavers that the vertebral system of veins drains not only the vertebrae but also the bones of the pelvic girdle and the upper ends of the femurs the bones of the shoulder girdle and the upper ends of the humeri and the skull This venous system is without valves, except in minor connecting channels The pressure within it is low Retrograde flow of blood occurs easily within it Indeed the blood surges back and forth

benign, that are growing rapidly demand an increased blood supply, and the prominent regional superficial veins are a manifestation of this increased blood supply

There are three groups of deep veins carrying blood from the breast and chest wall which are of special interest to us

1 The *perforating branches of the internal mammary veins* are the largest veins carrying blood from the breast Those in the upper three interspaces are larger than those in the lower interspaces



Fig 22 Superficial veins of the anterior chest wall as shown in infrared photograph Longitudinal type of pattern

The internal mammary veins empty into the corresponding innominate veins This venous pathway leads, of course, directly to the pulmonary capillary network, and provides a route for metastatic carcinoma emboli to the lungs

2 The *axillary vein receives many tributaries* from the chest wall, the pectoral muscles, and the deep surface of the breast In general they correspond to the branches of the axillary artery They are, however, more variable in their arrangement The tributaries entering the axillary vein are indeed so irregular that it is not worth while attempting to identify them, with the exception of the cephalic and thoraco-acromial veins

The axillary vein itself shows great variation The junction of the basilic and brachial veins to form the axillary vein may take place at any point from the outer edge of the teres major up to the clavicle When this junction occurs high up the axillary vein is in effect double. Care must be exercised not to mistake in such cases the main venous trunk from the arm for a large branch of the axillary vein coming from the lateral chest wall When in the course of an axillary dissection tension upon the specimen in a caudad direction bows the axillary vein downwards its relationships may be distorted Normally it lies medial (caudad when the arm is abducted as in an axillary dissection) to the axillary artery overlapping it so thoroughly that the artery is not seen at all during the dissection

A phenomenon which sometimes confuses the surgeon during his dissection of the axillary vein is the marked contractility of its lateral portion When the vein is first exposed it has a large caliber throughout its whole extent, although tapering somewhat toward the arm Dissection of the medial portion of the vein changes its caliber very little but dissection of the lateral half produces such sharp contraction of that portion of the vein that the surgeon may momentarily doubt that he is still dealing with the axillary trunk

The venous pathway from the breast through the axillary vein leads of course, directly to the pulmonary capillary network and provides a second route to the lungs for carcinoma emboli.

3 The third and one of the most important routes of venous drainage from the breast is directed posteriorly through the *intercostal veins* These veins communicate with the vertebral veins and finally empty into the azygos vein This route through the intercostal and azygos veins leads to the superior vena cava and to the lungs It constitutes a third pathway by which carcinoma emboli produce pulmonary metastases

These three venous routes for metastases from breast carcinoma to the capillary network of the lungs are shown especially in Figure 23

The vertebral system of veins provides an entirely different route by which metastases reach the bones directly without going through the caval veins and through the lungs

The vertebral veins constitute a separate vertical system of veins paralleling the caval system They drain blood from the vertebral column adjacent muscles and spinal cord They form intricate venous plexuses both inside and outside the vertebral canal extending along its entire length The so-called basivertebral veins form wide tortuous channels within the vertebral bodies similar to those in the diploë of the cranial bones, and empty into the anterior external vertebral plexus The vertebral plexuses communicate at each vertebral segment with the intercostal veins Figure 24 shows this communication as pictured in Gray s Anatomy

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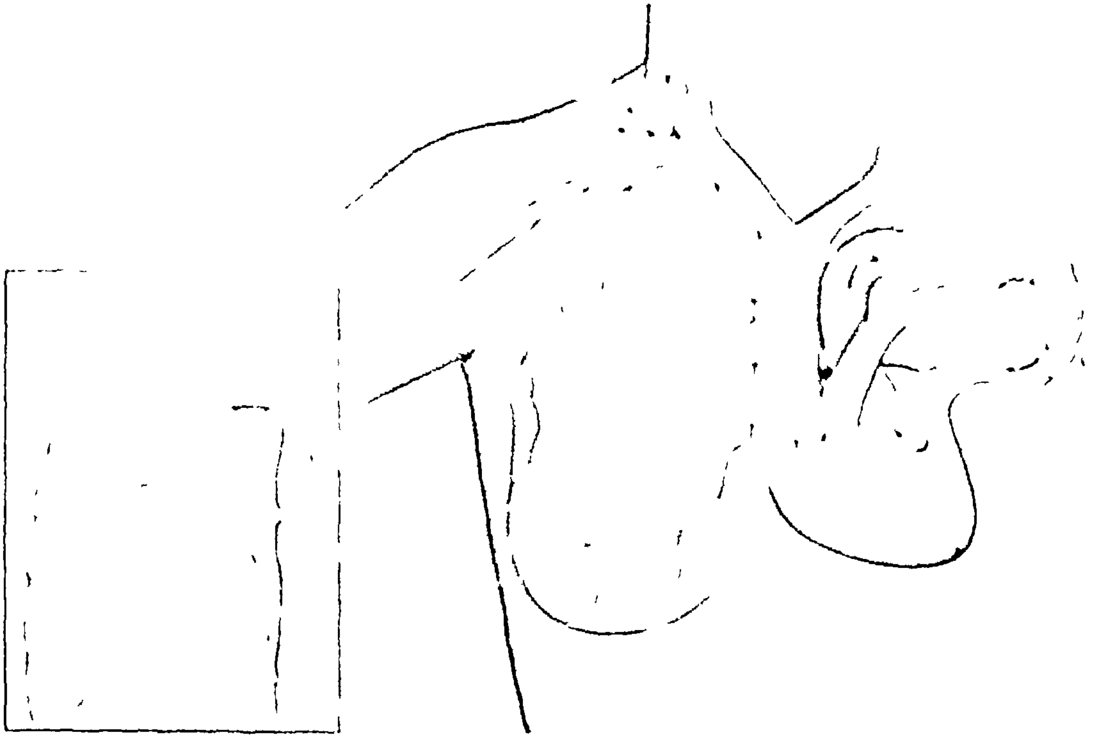


Fig 23 The three venous routes of metastasis from carcinoma of the breast to the capillary network of the lung shown diagrammatically

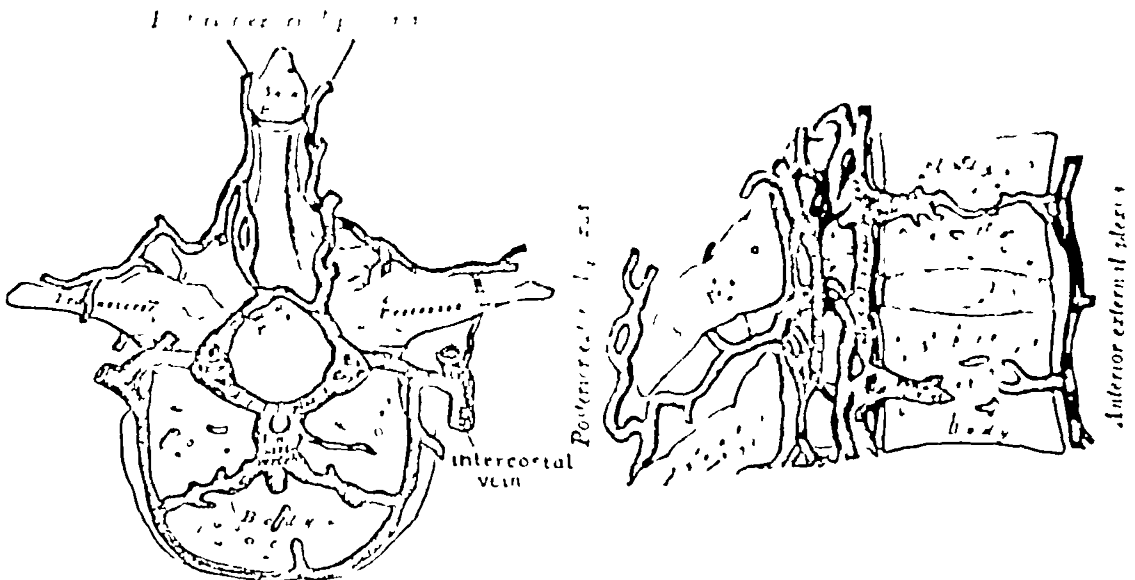


Fig 24 Transverse section of a thoracic vertebrae showing the vertebral venous plexuses and their communication with an intercostal vein (Gray s Anatomy, 26th ed , edited by Charles M Goss, M D , Courtesy of Lea & Febiger, 1954)

from the vertebral to the caval system with slight changes in intra-abdominal pressure The vertebral system can be readily injected through the tributaries of the caval system Figure 25 shows the vertebral plexus well outlined in an injection made into the femoral vein, in an autopsy study

Batson emphasizes that the vertebral system of veins provides a venous pathway in the long axis of the body along which metastases, escaping through the

intercostal veins draining carcinoma of the breast may spread to the skeleton without entering the caval venous system The frequency with which metastases are seen in the vertebrae, and in the pelvic bones, and skull without evident parenchymal pulmonary metastases, strongly supports the argument that the vertebral system of veins is an important route along which breast carcinoma metastasizes

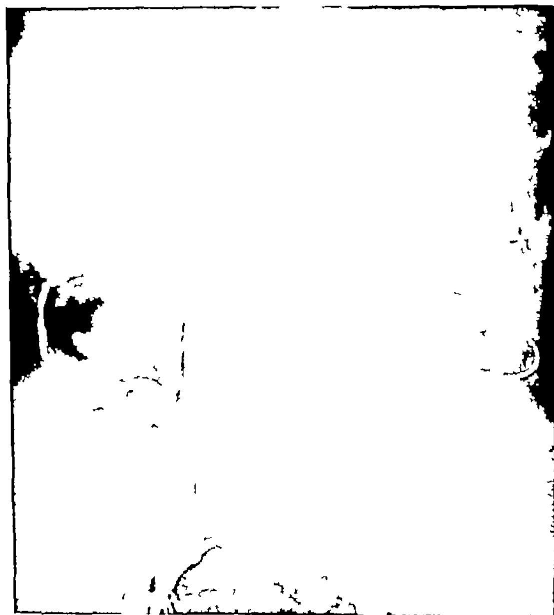


Fig 25 The vertebral plexus outlined by an injection into the femoral vein at autopsy

The Nerves of the Mammary Region

The skin over the upper part of the breast is supplied by the third and fourth branches of the cervical plexus

The skin of the lower part of the breast is supplied by the *thoracic intercostal nerves* Their lateral cutaneous branches emerge between the digitations of the serrati muscles in the anterior axillary line and supply the lateral breast skin Their anterior cutaneous branches emerge from the pectoralis major muscle with the perforating vessels close to the sternum and supply the medial breast skin

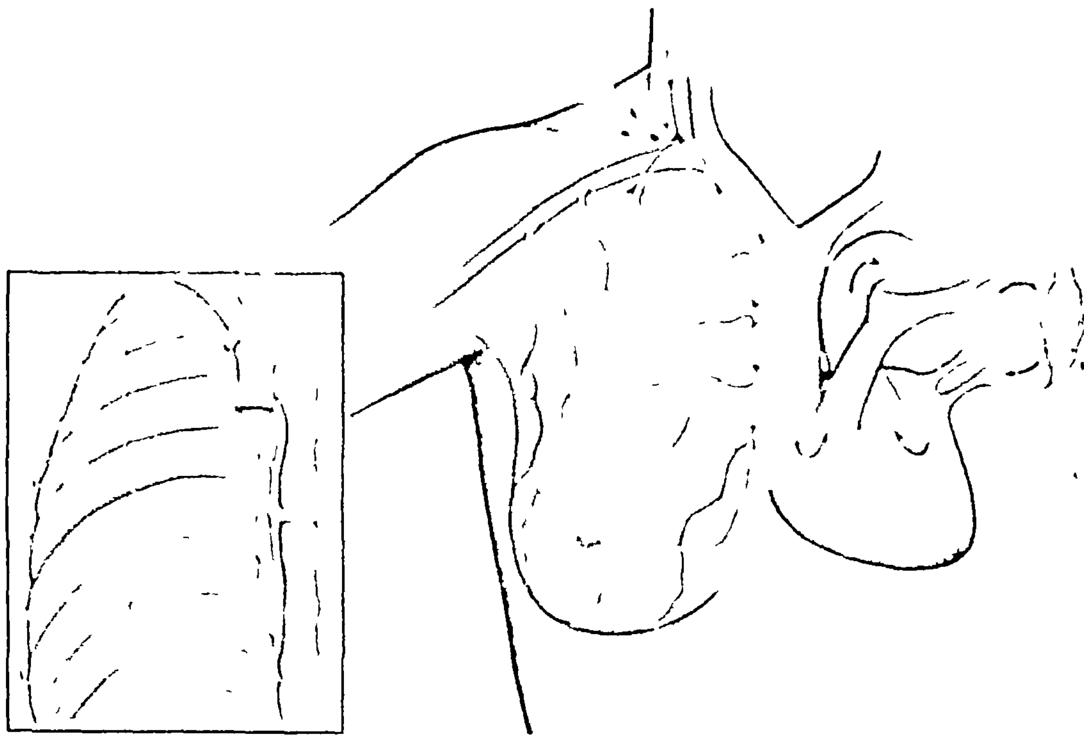


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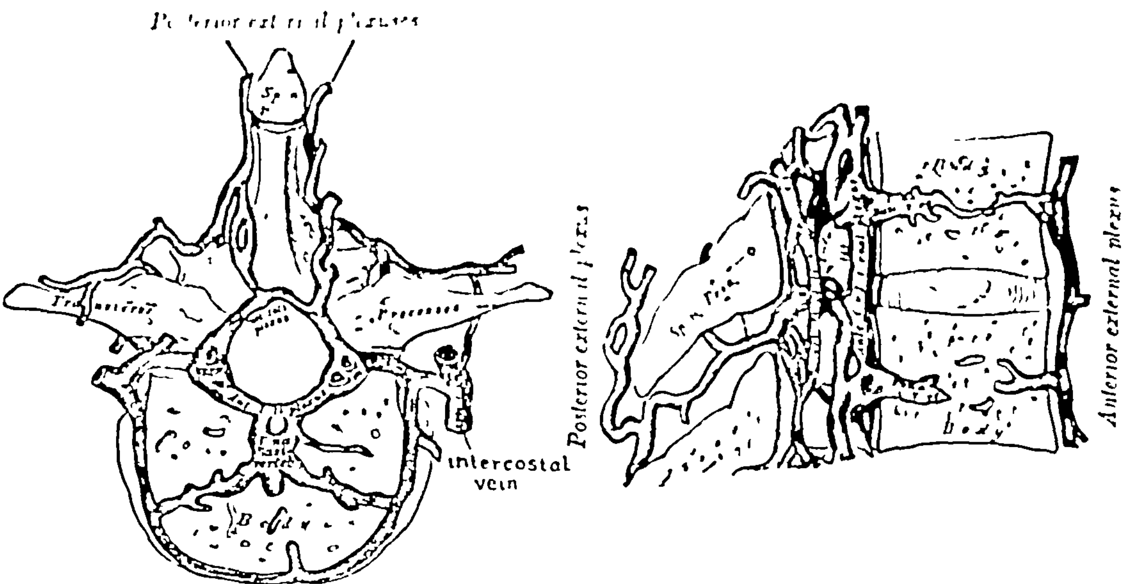


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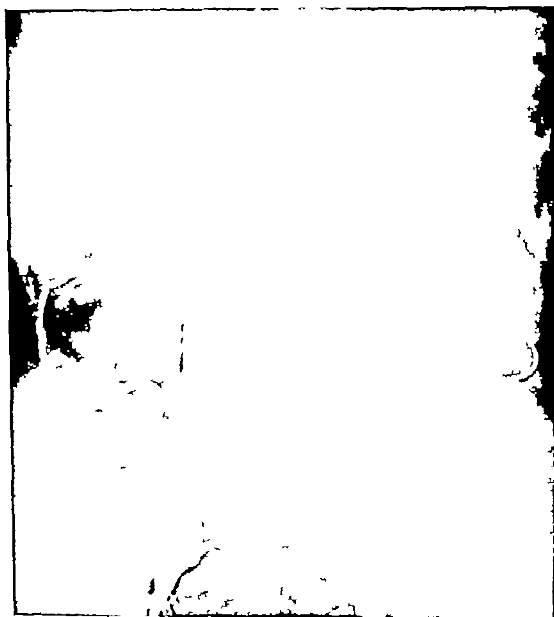


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areolar tissue to be removed in the dissection as its lateral wall In the depths of this cleft the long thoracic nerve will be seen lying in the fat which the dissection has peeled off of the serratus digitations. This nerve should not be sacrificed for lymph nodes are not ordinarily seen along or medial to it It should be freed displaced medially and left intact

The Lymphatics of the Breast

A knowledge of the lymphatic pathways from the breast is essential to an understanding of the natural course as well as the treatment of breast carcinoma Toward the end of the last century when surgeons began to extend the scope of the operative attack upon breast cancer some of them particularly Heidenhain in Germany and Stiles in Scotland made special studies of the lymphatic drainage of the breast Really thorough investigations with modern injection techniques were not made until some years later Oelsner (1901) working in Breslau, and Mornard (1916) working in Rouvière s laboratory in Paris, made the most important contributions to our knowledge of the subject Rouvière has summarized the knowledge of the whole subject in his book

A description of the lymphatics of the breast must begin with an account of the lymphatics of the skin over it. In the skin of the body as a whole there are no lymphatics in the epidermis itself In the dermis, however there are two networks of them, a narrow meshed superficial one without valves that sends branches up around the papillae and a wide meshed deeper one made up of broader channels equipped with valves that communicate with the subdermal lymphatics as well as the deeper lymphatics of the underlying fascia by means of vertical branches The breast is derived embryologically from the ectoderm and is therefore in a sense an organ of the skin It is situated between the lymphatics of the overlying dermis and the deep lymphatics of the underlying fascial plane and it has intimate lymphatic connections with both sets of lymphatics

Sappey s well known portrayal of a mercurial injection of the lymphatics of the skin of the chest wall including the mammary region (Fig. 26) shows the dermal lymphatics very well but is not entirely correct for our purposes, since it shows a male subject. It is, however worth reproducing to emphasize two points The first point is the striking directional lymphatic flow to the axilla from the whole upper anterolateral chest The second point is the watershed, at the umbilical level between drainage from the chest wall and the upper abdominal wall to the axilla and drainage from the lower abdominal wall to the groin A carcinoma of even the most caudad portion of the breast involving the skin of the inframammary region therefore drains into lymphatics which run to the axilla and not to the groin

The lymphatics of the mammary gland itself originate from a delicate lymphatic network around the mammary lobules. Collecting lymphatics follow the mammary ducts centripetally to the nipple region and there empty into the subareolar lymphatic plexus This plexus is a coarse meshed network of larger collecting lymphatics, originally pictured and described by Sappey (Fig. 27) It lies superficially upon the breast just beneath the areola. Out beyond the edge of the areola the subareolar plexus becomes less and less dense its interstices widen, and it forms a circumareolar plexus Grant and his associates in recent

injection studies made with Evans blue dye, have confirmed the existence of the subareolar plexus

Surgeons like myself, however, who have often seen breast carcinoma invading the pectoral fascia beneath the breast when there is no evidence of extension of the disease to the subareolar area, have doubted that the main direction of lymphatic drainage in the breast is centripetally toward the subareolar plexus It would seem more likely that lymphatics running vertically downward carry



Fig 26 The lymphatics of the skin of the anterior chest wall according to Sappey

carcinoma emboli to the lymphatics of the deep fascial plane Fraser found good evidence of this route of spread in his studies of the pathology of breast carcinoma, to which I shall refer in Chapter 18 More anatomical studies of the routes of lymphatic drainage from the breast are needed to settle this question

Lymphatic Pathways from the Breast to the Axilla

According to Rouvière two "enormous" collecting trunks originate from the periphery of the subareolar plexus, one laterally and one medially, and run to the axilla (Fig 28)

1 An *external trunk* runs laterally from the subareolar plexus to reach the outer border of the pectoralis major This external trunk receives collaterals from the upper half of the breast

2 An *internal trunk* from the medial edge of the subareolar plexus curves downward around beneath the areola to reach the outer border of the pectoralis major This internal trunk receives collaterals from the lower half of the breast

These two collecting trunk lymphatics pass around the outer edge of the pectoralis major muscle, penetrate the axillary fascia to enter the base of the axilla and terminate in the axillary lymph nodes

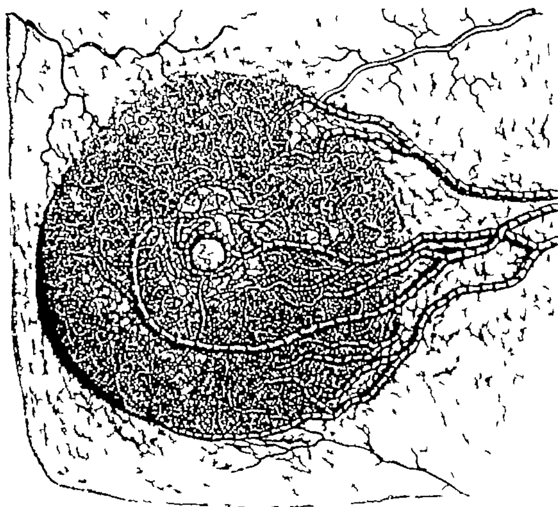


Fig 27 The subareolar lymphatic plexus (Sappey)

Although the main route of lymphatic drainage from the breast to the axilla is through this route, there are two accessory routes of lymphatic drainage from the breast which lead directly to the nodes at the apex of the axilla, as follows

1 *The transpectoral route* On the deep aspect of the breast, collecting lymphatics from a retromammary plexus in the loose areolar tissue between the pectoral fascia and the breast perforate the pectoralis major following the course of the pectoral branch of the thoraco-acromial artery and finally empty into the subclavicular group of axillary lymph nodes The importance of this transpectoral lymphatic route was first emphasized by Grossman and by Rotter Rotter found lymph nodes, which often contained metastases, on the posterior

aspect of the pectoralis major muscle or within its substance in about one-third of a series of operative specimens in which he had removed the pectoral muscles together with the breast and axillary content This fact made Rotter an early advocate, together with Halsted and Watson Cheyne, of removal of the pectoral muscles These lymph nodes occasionally found between the pectoralis major and minor muscles are therefore called, quite appropriately, "Rotter's nodes" Mornard could not demonstrate this transpectoral route in his thorough injection experiments

2 *The retropectoral route* In a considerable proportion of subjects (35 per cent according to Mornard) there exists a separate set of two or three collecting lymphatic trunks which drain the superior and internal portion of the breast

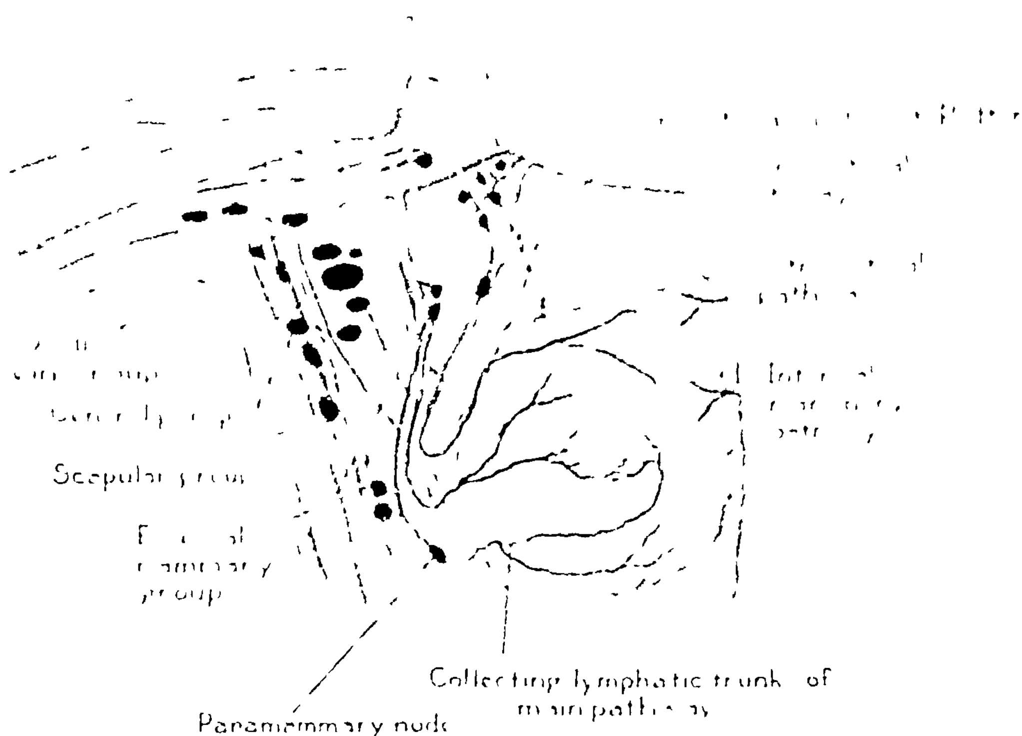


Fig 28 The pathways of lymphatic drainage from the breast (Modified from Rouviere, Anatomie des lymphatiques de l homme, Paris 1932)

These lymphatics proceed laterally to round the free margin of the pectoralis major, and then run upward and medially between the pectoralis major and minor, or beneath the minor, to the apex of the axilla, where they empty into the subclavicular group of lymph nodes Occasionally small lymph nodes occur in the course of these lymphatics of the retropectoral route beneath the pectoralis major Mornard believed that this is a better explanation of the occurrence of "Rotter's nodes" than a transpectoral lymphatic route Whichever explanation for the occurrence of "Rotter's nodes" is the right one remains problematical, but the reality of these interpectoral lymph nodes is beyond question We have occasionally encountered them in operating for breast carcinoma Their existence is one of the anatomical facts which necessitates removal of the pectoral muscles for breast carcinoma

The retropectoral route is a more direct pathway to the subclavicular nodes

than the main lymphatic route through the external mammary and central groups of axillary lymph nodes and offers one explanation for the bad prognosis of carcinoma situated in the upper inner sector of the breast.

When the axillary contents as removed in radical mastectomy are studied in a casual fashion as is the custom in many pathology laboratories and only the larger and obvious lymph nodes picked out for sectioning, from 5 to 10 lymph nodes only will be found Such a report usually means merely that the pathologist has failed to find the smaller nodes, for there are usually from 30 to 60 or more nodes It takes at least an hour of patient and systematic search to dissect them out of the axillary fat If the surgeon has not done a thorough axillary dis section the number of nodes will of course nevertheless, be small

In Dr Stout s laboratory this kind of meticulous search for all lymph nodes in the axillary portion of the radical mastectomy specimen has been carried out for many years The average number of lymph nodes per specimen found by the dissection method in a recent series of 75 consecutive cases, as shown in Table 1 was 21 5 Forty nine per cent of the cases had involved nodes In these cases an average of 7 5 nodes per case was found to contain metastases

Table 1 Dissection vs. Clearing Technique for Axillary Lymph Nodes in Consecutive Series of Cases

(Presbyterian Hospital—Pickren)

Method of search	Number of cases	Per cent of cases with involved nodes	Average number of involved nodes per case	Average number of nodes per case
Dissection	75	49 3	7 5	21 5
Cleared	196	53	6 3	37 3

In 1948 Monroe applied the clearing technique to the study of lymph nodes in a series of 87 radical mastectomy specimens In this method the axillary fat is rendered transparent, making it possible to identify very small nodes Monroe found an average of 30 4 nodes per specimen with this technique

In Dr Stout s laboratory the clearing method has been adopted for studying axillary lymph nodes since 1951 In a recent series of 196 cases studied in this manner by Pickren (Table 1) an average of 37 3 nodes per case was found An average of 6 3 nodes per case was found to contain metastases Fifty three per cent of the cases had involved nodes These data leave no doubt as to the greater accuracy of the clearing technique as compared with the dissection technique for studying radical mastectomy specimens

The clearing technique as it is now carried out in our laboratory of surgical pathology follows

The axillary fat and the fascia lying between the pectoralis major and pectoralis minor muscles are dissected away from the breast and muscles This axillary tissue is pinned out on a cork board and fixed in Kaiserling solution for twelve hours It is then placed in 80 per cent alcohol and incubated at 62 C for eight to twelve hours followed by immersion in 95 per cent alcohol at 62 for eight to

twelve hours then absolute alcohol at 62 C for eight to twelve hours In-between changes of the alcohols, the tissue is forcefully squeezed by hand to express the liquefied fat

After this dehydration process the tissue is placed in toluol for two hours to dissolve out the remaining fat The excess toluol is squeezed out of the tissue and it is placed in the cedarwood oil which clears it As the tissue lies in the cedarwood oil in a glass tray, a strong light is directed through it from below The lymph nodes are then easily dissected out and plotted on a diagram according to their location in the axillary specimen

Although the larger axillary lymph nodes in patients in older age groups show a considerable degree of replacement of the lymphoid tissue by fat, so that only a narrow rim of lymphoid tissue remains, the actual number of nodes found does not decrease in old age This fact is indicated in Table 2

Table 2 Number of Axillary Nodes in Relationship to Age (Presbyterian Hospital Pickren)

Age	Number of cases	Average number per case
31-35	3	37.0
36-40	6	29.8
41-45	7	39.5
46-50	14	31.0
51-55	5	36.2
56-60	7	42.0
61-69	4	38.5
70- over	4	34.5
	50	35.3

Mornard divides the axillary lymph nodes into five principal groups, as follows

1 *The External Mammary Group* The external nodes lie along the medial wall of the axilla, outside of or in the fascia covering the digitations of the serratus anterior muscle The chain extends from the sixth rib to the axillary vein, following the course of the lateral thoracic artery

Occasionally there are several small lymph nodes, the so-called paramammary nodes, interspersed in the course of the collecting trunk lymphatics from the breast to the external mammary group of nodes These paramammary nodes lie superficially just beneath the skin along the lateral edge of the pectoralis major

2 *The Scapular Group* The chain of scapular nodes lies along the subscapular and thoracodorsal blood vessels and extends from the lateral thoracic wall to the axillary vein

3. *The Central Group* The central group are the largest of the axillary nodes and they lie embedded in fat in the center of the axilla They are the nodes most often palpable They can best be felt by gentle palpation against the lateral thoracic wall with the arm relaxed and adducted, for in this position the deep pectoral fascia is relaxed and the nodes lie against the chest wall

4 *The Axillary Vein Group* The axillary nodes lie along the lateral portion of the axillary vein, usually on its caudad aspect

5 *The Subclavicular Group* The subclavicular nodes lie at the apex of the axilla They are often found as high as the surgeon can carry the dissection at the point where the subclavian vein disappears beneath the subclavius muscle The collecting trunks from all the other groups of axillary nodes empty into these subclavicular nodes and from the plexus of lymphatic vessels which connects them one with another one or more large lymphatic trunks arise which pass upward beneath the clavicle to empty into the junction of the jugular and subclavian veins These large trunks can be plainly seen at the very apex of the axilla, especially when the nodes contain metastases and the lymphatic trunks are enlarged

All the nodes which we have been describing lie beneath the costocoracoid fascia which encloses them together with the axillary blood vessels, nerves connective tissue, and fat within a delicate yet strong sheath This fascia gives coherence to the fat and lymph nodes of the axilla and makes their removal in one piece together with all the fascia easier than would otherwise be the case

From Pickren s studies with the clearing technique the actual number of lymph nodes in each of these anatomical groups is now available for the first time These data are shown in Table 3

Table 3. Numbers of Nodes in the Axillary Node Groups

(Presbyterian Hospital—Pickren)

Node group	*63 cases with axillary metastasis* Total number of nodes found	Average number	*62 cases with no axillary metastasis* Total number of nodes found	Average number	*Total (125 cases)* Total number of nodes found	Average number
1 Subclavicular	238	3 8	197	3 2	435	3 5
2. Axillary vein	891	14 1	753	12 1	1644	13 2
3 Central	775	12 3	626	10 1	1401	11 2
4 Scapular	445	7 1	344	5 5	789	6 3
5 External mammary	89	1 4	87	1 4	176	1 4
6 Interpectoral	134	2 1	81	1 3	215	1 7
Total	*2573	40 8	2088	33 7	*4661	37 3

* Total includes one case not assignable to node groups.

From these data it is apparent that the axillary vein group of nodes is the most numerous and the central group the next most numerous in the axillary filter The external mammary nodes are the least numerous

The axillary lymph nodes are so interconnected that they act as a series of filters interposed between the breast and the venous circulation Emboli of carcinoma cells must in most instances get through two or three groups of lymph nodes before they reach the venous circulation Thus the two main collecting lymphatic trunks from the breast run laterally and empty into the external mammary scapular and central groups of nodes Efferent lymphatics from these nodes connect with the axillary vein group of nodes From all these groups of

nodes efferent lymphatics empty into, or pass through, the subclavicular group of nodes at the apex of the axilla

From the subclavicular group of nodes two or three large lymphatic trunks pass medially through the small triangular space formed by the subclavian vein, the subclavius muscle tendon, and the chest wall These subclavian lymphatic trunks are large enough to be easily visible grossly if the surgeon keeps his operative field dry They should be identified and clamped, cut, and tied when an axillary dissection reaches the level of the subclavius muscle tendon, the highest point to which a standard axillary dissection is carried

The subclavian lymphatic trunks are very short In a study of autopsy specimens at the Delafield Hospital, Ju found that the distance from their origin from the highest axillary nodes to their termination at the jugular-subclavian venous confluence averaged only 3 cm The subclavian lymphatic trunks terminate in three ways (1) They may empty directly into the angle of union of the subclavian and jugular veins (2) They may join the jugular and bronchomediastinal lymphatic trunks to form a common lymphatic duct which then empties into the jugular-subclavian venous confluence (3) They may empty into sentinel lymph nodes of the supraclavicular (inferior deep cervical) group, situated close to the venous confluence

Keeping in mind the proximity of the subclavicular group of lymph nodes to the termination of this lymphatic pathway in the venous circulation, it is understandable why patients who are found to have metastases in the highest group of axillary lymph nodes are not cured by radical mastectomy They always eventually prove to be harboring visceral or bone metastases This, at least, has been our clinical experience

The Supraclavicular Lymph Node Group

The supraclavicular lymph nodes, the lowest of the group generally known as the inferior deep cervical lymph nodes of the neck, lie embedded in areolar tissue and fat beneath the platysma muscle above the clavicle These nodes occupy a triangle bounded medially by the internal jugular vein, caudad by the subclavian vein, and laterally by the trapezius muscle The floor of the triangle is the anterior scalene muscle

The most constant of the supraclavicular nodes are a sentinel group of nodes situated close to the angle of confluence of the internal jugular vein and the subclavian vein These nodes lie deeply beneath the lateral edge of the lower end of the sternocleidomastoid muscle behind the clavicle, and are a common site for metastasis from breast carcinoma They are too deeply placed to be palpable unless much enlarged In addition to these sentinel nodes, there are usually one or two nodes situated more cephalad upon the internal jugular vein or the anterior scalene muscle, and several nodes situated more laterally along the subclavian vein or between it and the artery, and upon the brachial plexus A total of 10 or 12 nodes are usually removed in a supraclavicular dissection The nodes that are palpable clinically when involved by carcinoma are usually the more lateral and more superficially situated ones When these nodes are enlarged it must be assumed that they have been involved by retrograde permeation of lymphatics connecting them with the deeply placed sentinel nodes which are the

first to be involved by metastases from the breast reaching this lymphatic terminus via the subclavian lymphatic trunks

There has been a difference of opinion among authorities as to the existence of a direct lymphatic pathway between the upper portion of the breast and the supraclavicular lymph nodes crossing superficial to the clavicle and by passing the axillary lymph node filter Mornard found such a route in 3 per cent of the subjects that he injected Neither Oelsner nor Rouvière was able to demonstrate this route, however and it is probably correct to assume that it does not exist.

From the sentinel nodes of the supraclavicular group situated near the jugular subclavian angle, collecting lymphatic trunks empty directly into the jugular subclavian venous confluence on the right side or into the thoracic duct in some subjects on the left side

Again keeping in mind the proximity of metastases in the supraclavicular lymph nodes to the point of entry of this lymphatic route into the venous circulation it is understandable why patients with such supraclavicular metastases may be assumed always to have metastases carried to viscera or bones by the blood stream

Lymphatic Drainage from the Breast to the Internal Mammary Nodes

Our knowledge of the anatomy of this lymphatic route is new and we owe it to surgeons rather than anatomists W Sampson Handley carried out comprehensive studies of the routes of spread of breast carcinoma during the early years of our century and became interested in the internal mammary route He encouraged the English anatomist Stibbe to make the first thorough study of the internal mammary lymphatics Based on 60 autopsies the study appeared in 1918

The collecting lymphatic vessels of the route drain the central and medial portions of the breast They follow the perforating blood vessels down through the pectoralis major muscle and empty into the internal mammary chain of nodes situated in the intercostal spaces at the edge of the sternum

The nodes lie beneath the internal intercostal muscle and beneath a delicate but definite fascia that forms a roof over the space in which the internal mammary artery and veins and the internal mammary lymphatic trunks with their lymph nodes lie embedded in areolar tissue (Fig 29) Sledziewski who made careful studies in 1931 and 1937 of the internal mammary lymphatics, found that there are usually two or three delicate lymphatic trunks on each side In the first, or first and second intercostal spaces the nodes lie upon and are separated from the parietal pleura only by a thin layer of fascia that Stibbe named the costo-sternal fascia and which has also been called the endothoracic fascia. This fascia is so thin that the lung can be seen moving beneath it In the lower interspaces this fascia is continuous with the transversus thoracis muscle which constitutes another layer of tissue between the internal mammary vessels and the pleura

The internal mammary nodes are small measuring usually only 2 to 4 mm in diameter Microscopical study often reveals additional minute foci of lymphoid tissue scattered along the course of the internal mammary vessels The grossly visible nodes are concentrated in the upper three interspaces and are often lacking in the lower three interspaces

The internal mammary nodes are situated in the interspaces between the costal cartilages, within 3 cm of the sternal edge. The firm attachment of the endothoracic fascia to the deep surface of the costal cartilages and the sternum normally prevents the nodes from lying behind the costal cartilages and behind the sternum, although a node may sometimes be partially concealed in the groove at the edge of the cartilage or at the edge of the sternum.

Stibbe found the average total number of internal mammary lymph nodes per subject, including both sides, to be 8.5. The typical distribution was four on one side and five on the other, with one node in the upper three interspaces on each

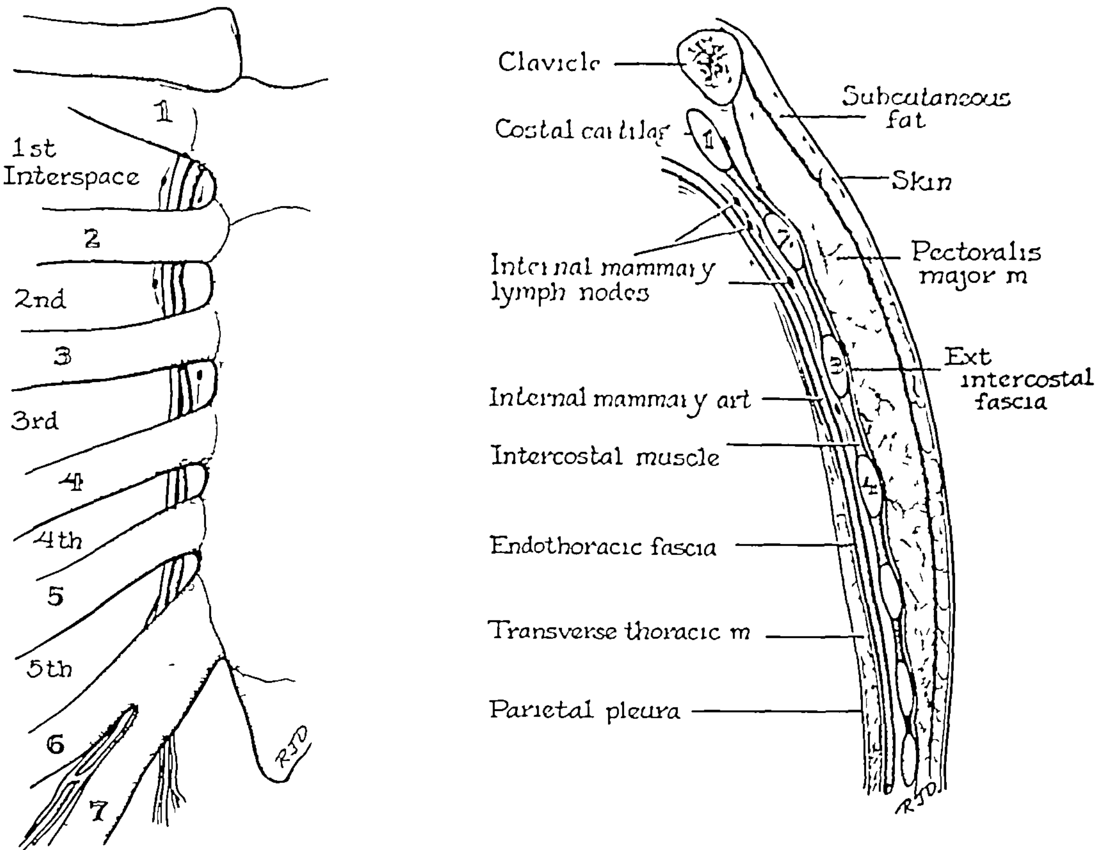


Fig. 29. The internal mammary lymphatics

side, one in the sixth space on each side, and an extra node in one of the upper spaces. Stibbe's findings of grossly visible nodes are summarized in his table.

Table 4. Total Number of Glands on Both Sides in 60 Subjects
(Stibbe)

Space	Contained no gland	One gland	Two glands	More than two
First	4	91	19	6
Second	3	91	24	2
Third	21	75	19	5
Fourth	109	11		
Fifth	105	15		
Sixth (or behind sixth cartilage)	45	75		

Soerensen at the suggestion of his surgical colleagues in Stockholm studied the arrangement of the internal mammary nodes in 39 autopsies He found an average total of 7 nodes per subject, or 3 5 on each side Soerensen emphasized a fact that is of fundamental importance to surgeons searching for them—namely their minute size He pointed out that the great majority of the normal nodes are only 1 or 2 mm in diameter while a few measure as much as 5 or 6 mm If the fat adjacent to the internal mammary vessels is removed when no

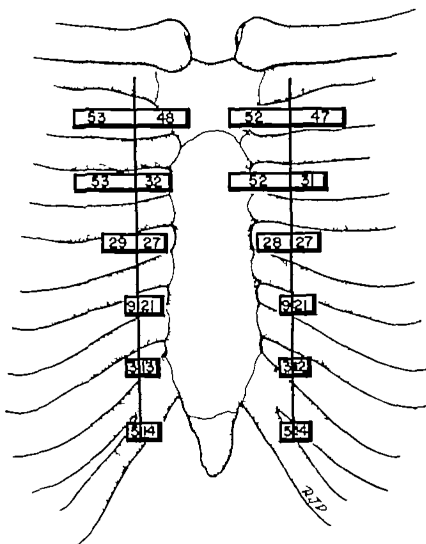


Fig 30 The distribution of the internal mammary nodes according to Ju

node can be identified grossly by the surgeon microscopical study will often reveal several small aggregations of lymphoid tissue

At the Francis Delafield Hospital David Ju investigated the number and position of the internal mammary nodes in a series of 100 autopsies. The sternum and costal cartilages were removed in one piece and the nodes subsequently dissected out He found an average total of 6 2 nodes per subject or 3 1 on each side Figure 30 shows the total numbers and arrangement of the nodes as Ju found them in 100 subjects Stibbe reported a marked concentration of these nodes in the upper three interspaces and in the sixth interspace Ju, on the other hand noted the same concentration of nodes in the upper three interspaces but

The internal mammary nodes are situated in the interspaces between the costal cartilages, within 3 cm of the sternal edge The firm attachment of the endothoracic fascia to the deep surface of the costal cartilages and the sternum normally prevents the nodes from lying behind the costal cartilages and behind the sternum, although a node may sometimes be partially concealed in the groove at the edge of the cartilage or at the edge of the sternum

Stibbe found the average total number of internal mammary lymph nodes per subject, including both sides, to be 8 5 The typical distribution was four on one side and five on the other, with one node in the upper three interspaces on each

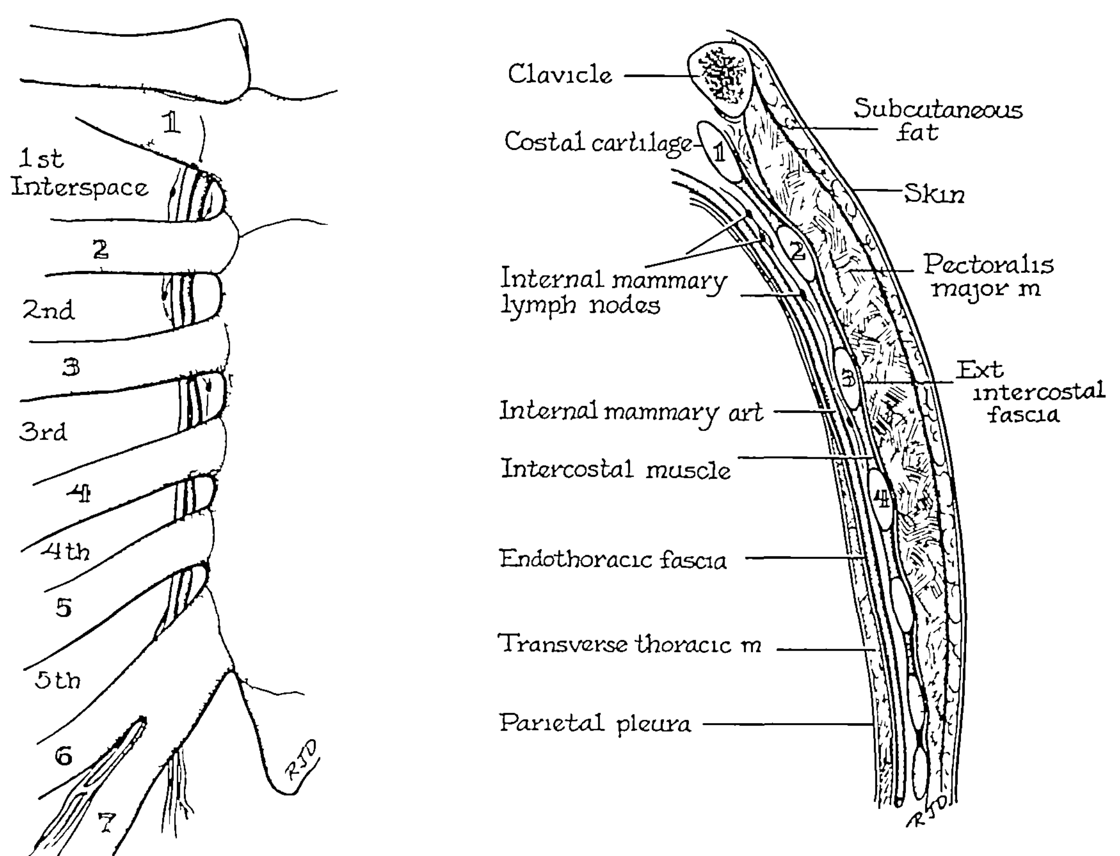


Fig 29 The internal mammary lymphatics

side, one in the sixth space on each side, and an extra node in one of the upper spaces Stibbe's findings of grossly visible nodes are summarized in his table

Table 4 Total Number of Glands on Both Sides in 60 Subjects (Stibbe)

Space	Contained no gland	One gland	Two glands	More than two
First	4	91	19	6
Second	3	91	24	2
Third	21	75	19	5
Fourth	109	11		
Fifth	105	15		
Sixth (or behind sixth cartilage)	45	75		

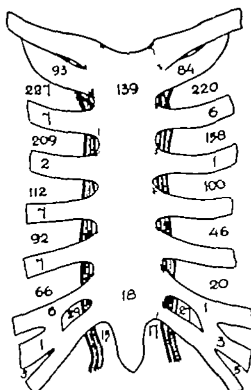


Fig. 31 The distribution of the internal mammary nodes according to Arão and Abrão

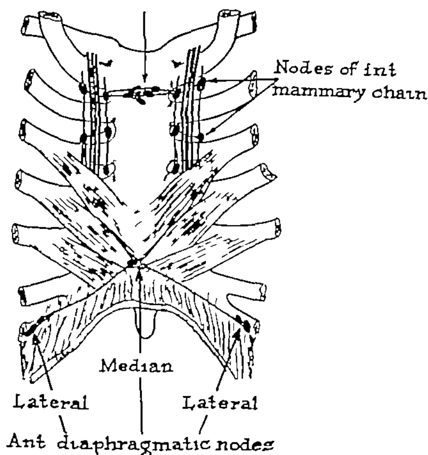


Fig. 32. Retromanubrial nodes according to Arao and Abrão

found that the lower three interspaces contained nodes infrequently but with about an equal incidence Another point of difference in Stibbe's and Ju's findings was that according to Stibbe most of the nodes found in the first and second interspaces were situated to the medial side of the internal mammary artery Ju found that they were about equally placed at each side of the artery My own experience with the nodes in the first interspace, which narrows sharply at the sternal edge and which is very difficult to explore in many patients because it is so narrow, is that this node is most often found lateral to the internal mammary vessels

In Rome, Putti, at the suggestion of Margottini, studied the number and arrangement of internal mammary nodes in 47 cadavers He found an average of 7 7 lymph nodes per subject The distribution of the nodes which he found was as follows

	%
1st intercostal space	91
2nd " "	89
3rd " "	70
4th " "	46
5th " "	12
6th " "	10
At the bifurcation of the internal mammary	23

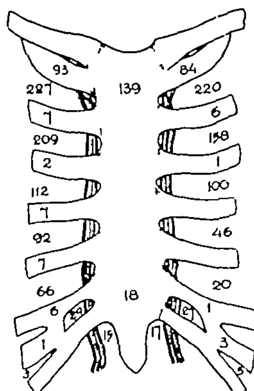


Fig 31 The distribution of the internal mammary nodes according to Arão and Abrão

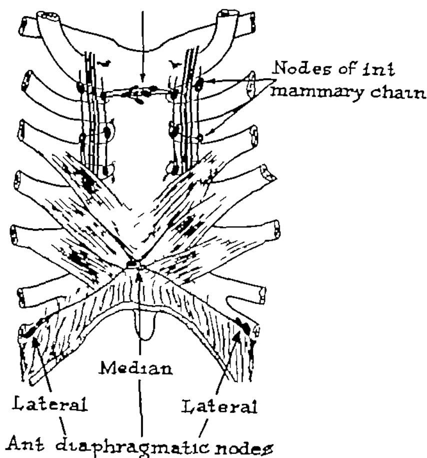


Fig. 32. Retromanubrial nodes according to Arão and Abrão

upper portion of the anterior abdominal wall supplied by the superior epigastric artery. This includes the upper portion of the rectus abdominis and the rectus sheath.

The internal mammary lymphatic trunks eventually empty into the great veins by one of several routes. They may empty on the left side into the thoracic duct, and on the right side into the right lymphatic duct. They may terminate on each side in the lowest lymph node of the inferior deep cervical group which lies just behind the medial end of the clavicle, and thence into the great veins. Finally, they may empty directly into the jugular-subclavian vein confluence. The important point is that once a metastasis from breast carcinoma reaches a lymph node of the internal mammary chain, in the first or second intercostal space, it is a very short distance from a point of entry into the venous circulation.

Lymphatic Drainage from the Breast to the Opposite Axilla

Occasionally, the lymphatics of the skin on one side of the sternum cross the midline and empty into the lymph nodes of the opposite axilla. Oelsner was able to inject such crossing lymphatics in two out of nine subjects. This route provides one explanation for metastases to the contralateral axilla in breast carcinoma. Another route for such contralateral metastases is through the deep pectoral fascia lymphatics beneath the opposite breast.

Lymphatic Drainage of the Muscles of the Chest Wall

The lymphatics which arise in the pectoralis major in general follow the course of the blood vessels which supply it. Those from its medial portion follow the perforating vessels into the internal mammary lymphatic route. Those from the remainder of the muscle terminate in the lymph nodes of the axilla, principally those of the external mammary group. The lymphatics from the pectoralis minor empty into the same group of lymph nodes.

The lymphatics from the fascia overlying the serratus magnus and from its superficial surface follow the branches of the thoracodorsal vein and empty into the axillary lymph nodes. There is another set of lymphatics from the deep surface of this muscle which communicate with the lymphatics of the external intercostal muscles.

The external intercostal muscles are drained by collecting lymphatics, two or three in each intercostal space, which follow the intercostal vessels around posteriorly. These collecting lymphatics empty into the posterior intercostal lymph nodes which lie in each interspace upon the inner aspect of the thoracic wall, close to the heads of the ribs. There are from one to three of these nodes in each interspace. They are shown in Figure 33, a diagram of the lymphatic drainage of the breast as seen in cross-section. In addition to the collecting lymphatics from the external intercostal route these nodes also receive efferent lymphatics from the parietal pleura, the vertebrae, and the spinal muscles. These connections of course provide a route for carcinoma emboli from the breast to reach the pleura or the vertebrae by retrograde permeation.

The efferent lymphatic vessels from the posterior intercostal nodes in the lower five or six interspaces run downward and unite to form a common collecting lymphatic trunk on each side, which empties into the thoracic duct (Fig. 34).

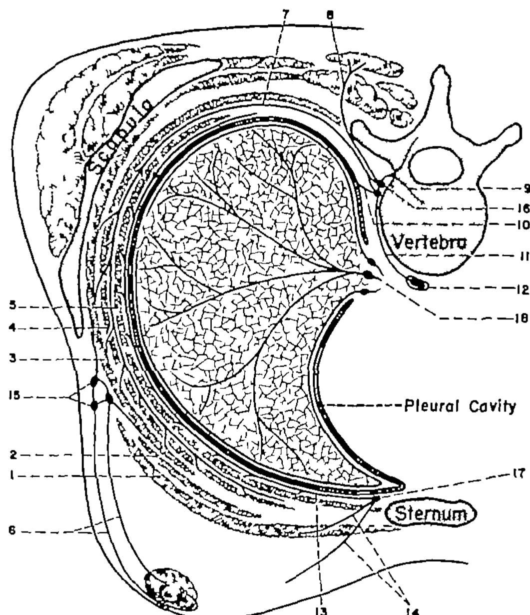


Fig 33 The lymphatic drainage of the breast in cross-section.

1 Pectoralis major m
2. Pectoralis minor m.
3 Serratus magnus m.
4 Ext. intercostal m
5 Int. intercostal m.
6 Lymphatics from breast to axillary lymph nodes
7 Ext. intercostal lymphatics
8 Lymphatics from spinal muscles
9 Lymphatics from vertebra
10 Lymphatics from parietal pleura
11 Lymphatics from post. intercostal lymph nodes to thoracic duct
12. Thoracic duct
13 Int. intercostal lymphatics
14 Lymphatics from breast to int mammary lymph nodes
15 Axillary lymph nodes
16 Post. intercostal lymph nodes
17 Int. mammary lymph nodes
18 Lymph nodes of pulmonary pedicle

The efferents from the posterior intercostal nodes of the first and second inter spaces usually run upward, behind the subclavian artery and either empty into a node of the inferior deep cervical (supraclavicular) group or join one of the other collecting lymphatic trunks and empty into the venous confluence This connection provides another route by which a metastasis from breast carcinoma can reach the supraclavicular lymph nodes

The efferents from the posterior intercostal nodes in the third, fourth, and fifth interspaces run transversely or obliquely and anastomose to form an irregular plexus lying upon the vertebral bodies. In this prevertebral lymphatic plexus there are interposed a number of juxtavertebral lymph nodes. From these nodes efferent lymphatic trunks empty into the thoracic duct.

The internal intercostal muscles are provided with lymphatics which run anteriorly in the respective intercostal spaces and empty into the internal mam-

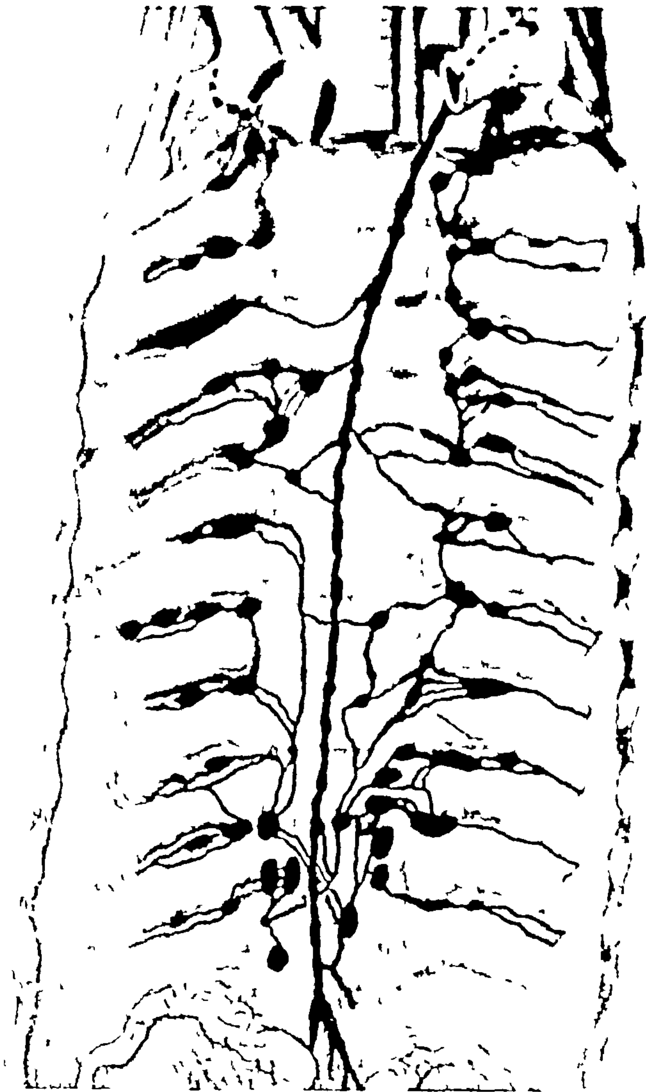


Fig 34 The posterior intercostal lymph node route (From Anatomie des lymphatiques de l'homme, H Rouviere, Paris, 1932, Fig 37, p 157)

mary lymphatic route These internal intercostal lymphatics also receive lymphatics from the parietal pleura

The Great Collecting Trunks of the Lymphatic System at the Base of the Neck

In our discussion of the pathways for metastases from breast carcinoma, we are particularly concerned with the lymphatic drainage of the breast and axilla, the anterior mediastinum, and the chest wall The collecting lymphatic trunks

from these areas all empty into the confluence of the internal jugular and subclavian veins at the base of the neck on each side, which may appropriately be called the *Grand Central Lymphatic Terminus* of the body (Fig 35) The details of the anatomy of the terminal collecting lymphatic trunks in this region are of great practical importance for us

There are essentially three groups of these *terminal lymphatic trunks* the subclavian, the jugular and the bronchomediastinal Earlier anatomists pictured

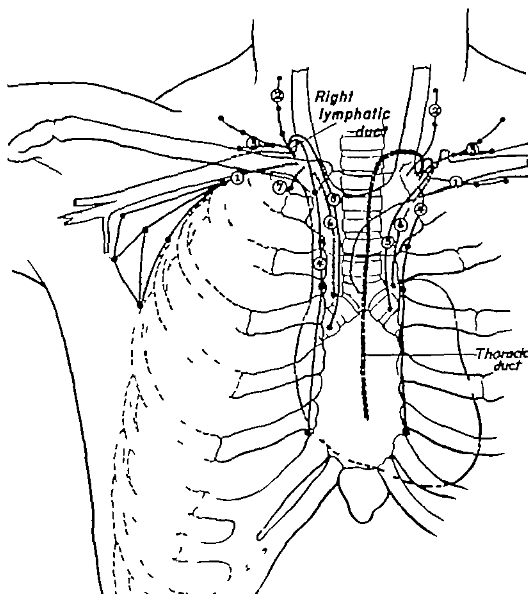


Fig 35 The great lymphatic trunks at the base of the neck.

these as single collecting trunks, but the recent studies of Rodrigues and Pereira in Rouvière's Parisian laboratory and of Sledziewski in Warsaw have shown them to be very irregular both as to number and as to the manner in which they combine and empty in the venous confluence Their findings can be summarized as follows with reference to Figure 35

1 The *subclavian trunks* (efferent from the axilla) are the most constant. There are usually two or three of them

2 and 3 Instead of a single *jugular trunk* (efferent from the neck and supra

The efferents from the posterior intercostal nodes in the third, fourth, and fifth interspaces run transversely or obliquely and anastomose to form an irregular plexus lying upon the vertebral bodies In this prevertebral lymphatic plexus there are interposed a number of juxtavertebral lymph nodes From these nodes efferent lymphatic trunks empty into the thoracic duct

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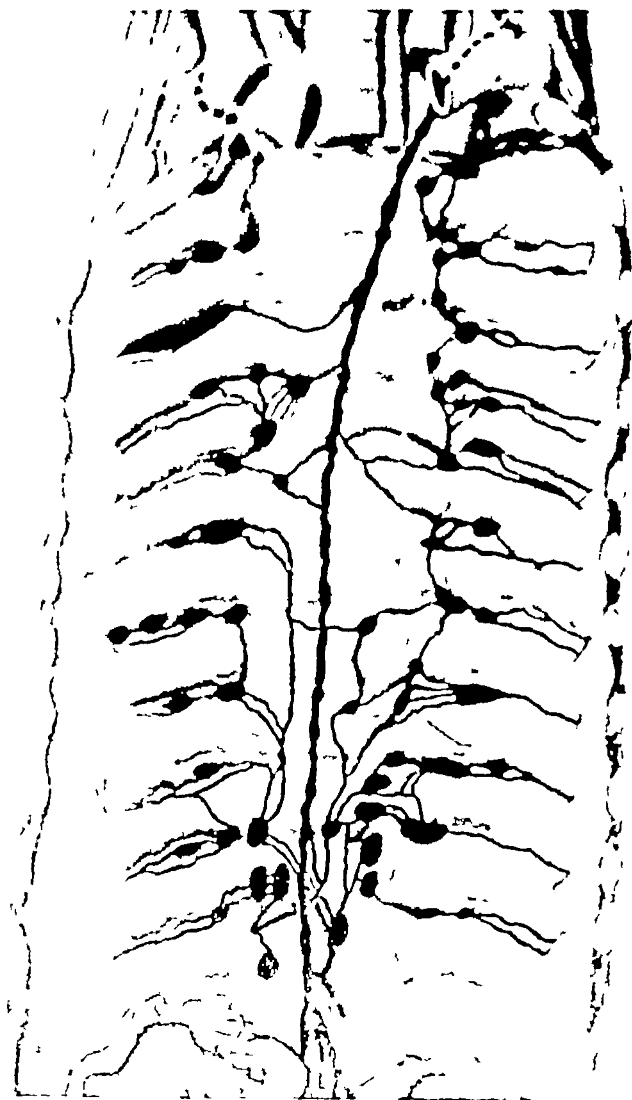


Fig 34 The posterior intercostal lymph node route (From Anatomie des lymphatiques de l homme, H Rouviere, Paris, 1932, Fig 37, p 157)

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clavian internal jugular and transverse cervical trunks are the ones which most often unite to form the common duct. More often however most of the trunks empty separately into the venous confluence

On the left side the various trunks empty either into the internal jugular vein into the subclavian vein or into the thoracic duct (Fig 37) The anterior mediastinal and the laterotracheal trunks are the ones which most often empty into the thoracic duct. The subclavian and internal mammary trunks are the ones which most often terminate independently in the great veins

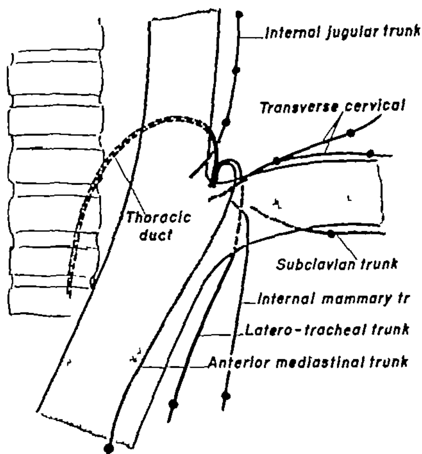


Fig 37 The termination of the great lymphatic trunks at the base of the neck on the left side

The lesson regarding carcinoma of the breast which must be inferred from this anatomy is that when emboli of carcinoma cells filter through the defense zone of axillary lymph nodes and reach the subclavian trunk, their route of escape into the venous circulation is short and easy Metastases into the internal mammary nodes are almost as close to this danger point It is unlikely that any surgical attack no matter how radical in scope or meticulous in detail, can hope to cure breast carcinoma that has reached the apex of the axilla or the internal mammary route, because metastases will have already escaped into the blood stream.

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Arão A. and Abrão A Estudo anatômico da cadeia ganglionar mamária interna em 100 casos. Rev paulista de med., 45 317 1954

clavicular areas) there are usually two or three collecting trunks from the internal jugular nodes, and one or two quite separate trunks from the transverse cervical chain of nodes (the supraclavicular nodes)

4 The *internal mammary trunks* run upward and terminate, quite independently of the other mediastinal trunks, in the venous confluence

5 The right *anterior mediastinal trunk* originates in nodes situated along the phrenic nerve and the anterior portion of the root of the right lung It runs upward anterior to the vena cava and empties separately into the right venous confluence The left *anterior mediastinal trunk* is pre-aortic, ascending from the anterior portion of the root of the left lung It empties into the terminal portion of the thoracic duct, or terminates separately in the left venous confluence

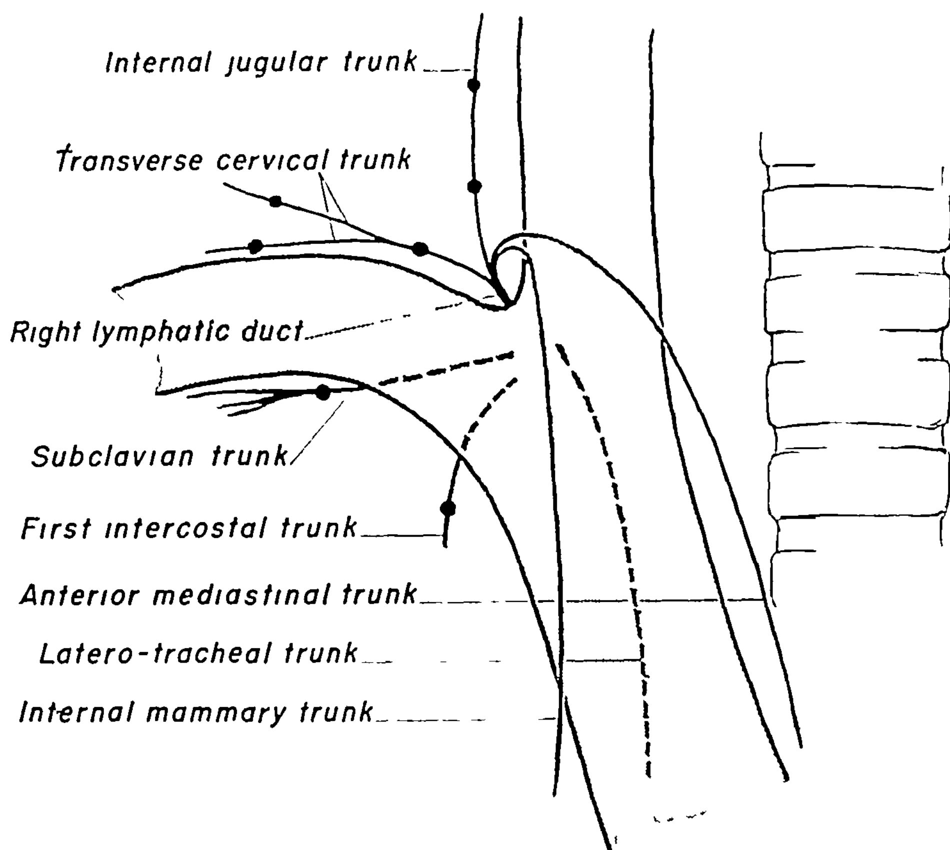


Fig 36 The termination of the great lymphatic trunks at the base of the neck on the right side

6 There are usually several trunks on each side from the *posterior mediastinal* and *laterotracheal* groups of nodes These trunks drain the roots of the lungs, ascend along the sides of the trachea, and empty into the venous confluence on each side

7 Finally, there is sometimes a short collecting trunk from the posterior intercostal lymph node of the first interspace which ascends behind the great vessels and empties into the venous confluence

All seven of these groups of collecting lymphatic trunks terminate finally in the confluence of the subclavian and internal jugular vein on each side In some subjects some of these trunks combine in a variety of ways on the right side to form a short common trunk called the right lymphatic duct (Fig 36) The sub-

clavian internal jugular and transverse cervical trunks are the ones which most often unite to form the common duct More often however most of the trunks empty separately into the venous confluence

On the left side the various trunks empty either into the internal jugular vein into the subclavian vein or into the thoracic duct (Fig 37) The anterior mediastinal and the laterotracheal trunks are the ones which most often empty into the thoracic duct The subclavian and internal mammary trunks are the ones which most often terminate independently in the great veins

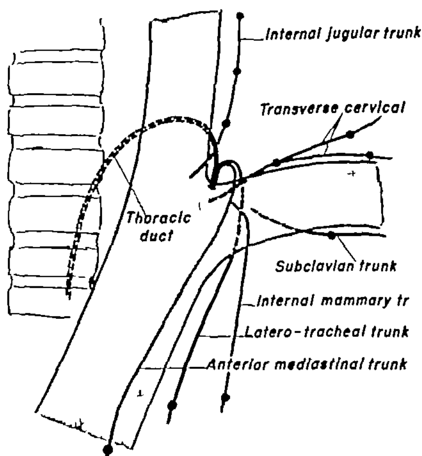


Fig. 37 The termination of the great lymphatic trunks at the base of the neck on the left side.

The lesson regarding carcinoma of the breast which must be inferred from this anatomy is that when emboli of carcinoma cells filter through the defense zone of axillary lymph nodes and reach the subclavian trunk, their route of escape into the venous circulation is short and easy Metastases into the internal mammary nodes are almost as close to this danger point It is unlikely that any surgical attack no matter how radical in scope or meticulous in detail can hope to cure breast carcinoma that has reached the apex of the axilla or the internal mammary route because metastases will have already escaped into the blood stream

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CHAPTER 2

THE PHYSIOLOGY OF THE BREASTS

The mammary glands are an integral part of the female reproductive system, and as such are subject to its hormonal control. The isolation during recent years of some of the hormones and their therapeutic use has taught us something concerning the physiology of the breast, but our knowledge is still very inadequate.

There are three types of physiological changes in the breast: (1) growth and involution, (2) the cyclical changes associated with menstruation, and (3) milk secretion. The anterior pituitary and the ovarian hormones directly or indirectly control these functions of the mammary glands.

Growth and Involution

The mammary glands develop in early embryonal life as a budding downgrowth from the ectoderm. By the time of birth the glands in the human being consist of a branching system of ducts emptying into a well developed nipple. The gland fields are not yet apparent.

Within a few days after birth, in a considerable proportion of babies of both sexes, there is evidence of some slight degree of secretory function. The rudimentary breasts appear to enlarge and there is slight secretion of a milky material from the nipples. This is no doubt due to lactogenic hormones in the maternal circulation before birth. After a week or so, this secretory activity subsides and the infantile mammary glands lapse into the inactive state which characterizes them during childhood. The epithelial elements consist merely of small ducts scattered throughout a fibrous stroma. Figure 38 shows such a breast from a 12 month old female child.

With the onset of puberty, between the tenth and fifteenth years, in the female, the breasts begin to grow, the areola enlarges, becomes more pigmented, and a discoid mass of breast tissue takes form beneath it. This increase in size of the breast is correlated with microscopical budding of the ducts to form gland fields. The breasts are often well developed by the time menstruation begins. Figure 39 shows the structure of the breast in a 14 year old girl.

The growth and maturation of the mammary gland is governed by ovarian and pituitary hormones. Both Riddle and Turner have written comprehensive reviews of present-day knowledge of this subject. *Estrogen* is clearly the chief stimulant of epithelial growth of the mammary gland. The administration of estrogen to immature or castrate animals in which the mammary gland is still

rudimentary causes the epithelium to proliferate and form a duct system with gland fields identical with that seen in normal mature animals When estrogen is given in continued and large doses to normal animals, a variety of types of epithelial proliferation of the mammary epithelium are produced depending upon the species and indeed upon the particular strain being used In mice in which most of these experiments have been done (Haagensen and Randall) the treated mammary glands of females of strains that have a high incidence of spontaneous mammary carcinoma show intense epithelial proliferation and some degree of cystic change In the strains that have a low incidence of mammary carcinoma cystic changes predominate In male mice of the high cancer strains the treated mammary glands also show marked epithelial proliferation This is slight or absent in the male mice of the low cancer strain



Fig 38 Normal mammary gland in a 12 month old female child

Speert showed that estrogen caused accentuation of the growth process of the mammary gland in rhesus monkeys and that this effect continued for as long as the treatment was maintained

In human beings the use of estrogen therapeutically in both sexes has provided abundant evidence which confirms the stimulative effect upon the mammary epithelium observed in animals Estrogen induces breast growth in castrated women (Werner and Collier) In any laboratory of surgical pathology breast tissue removed from women who have been given estrogen for a long time is occasionally seen today It shows a great variety of epithelial proliferation and cystic change Figure 40 illustrates irregular proliferation of the acinar epithelium and the formation of microcysts in a patient of ours who had been given estrogen over a long period of time In this case both breasts showed a great variety of

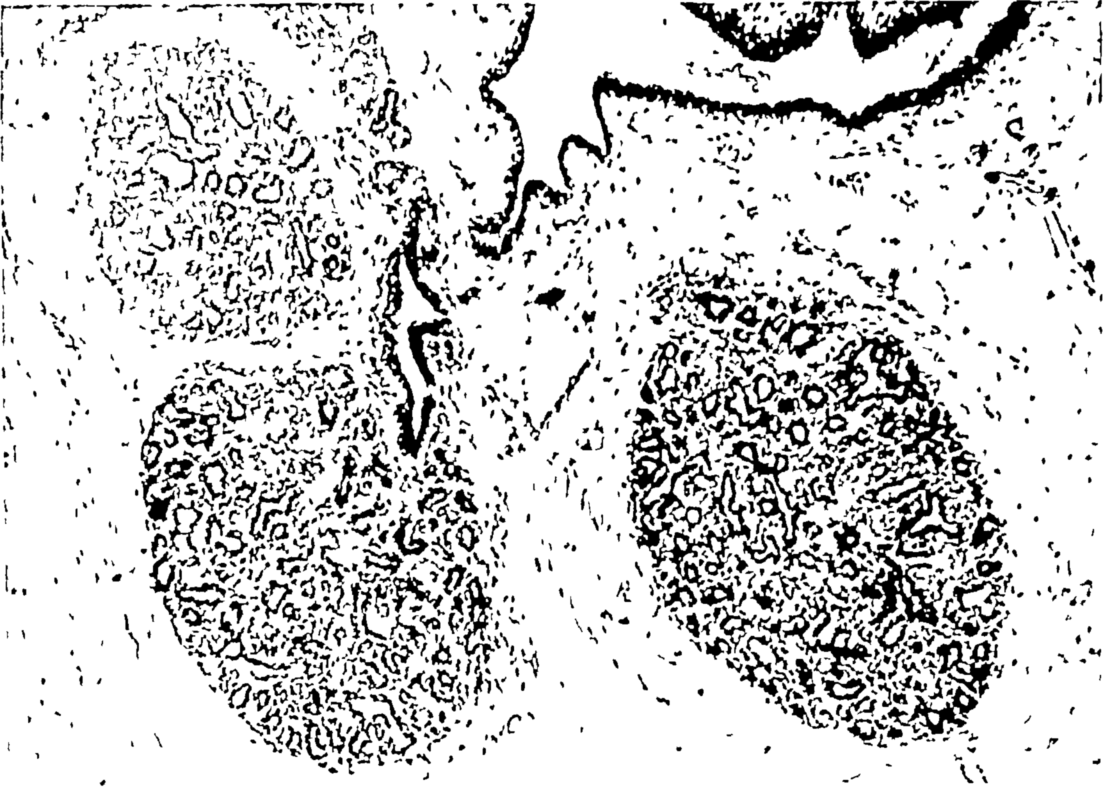


Fig 39 Structure of the breast in a 14 year old girl

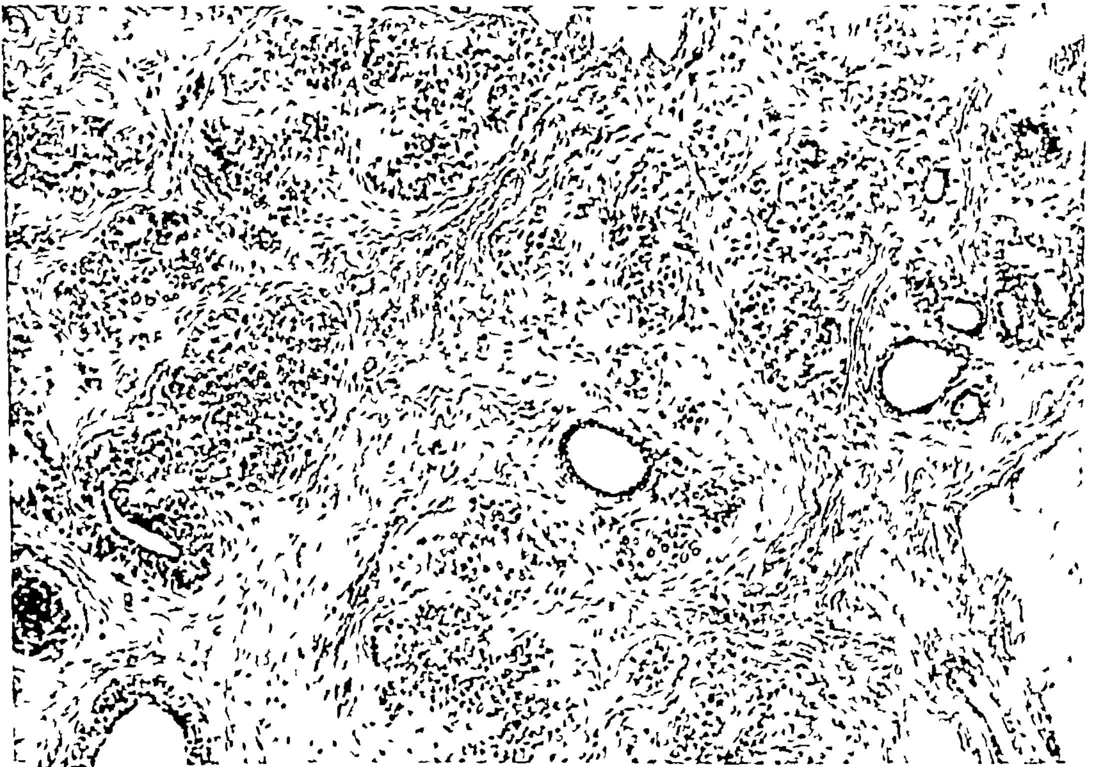


Fig 40 Epithelial proliferation and formation of microcysts in patient who had been given estrogen over a long period of time

types of epithelial proliferation some of which we illustrated in our published description (Auchincloss and Haagensen) Huseby and Thomas have recently published a good description of the microscopical changes in the breast produced by the therapeutic use of estrogen

Such epithelial proliferation has also been observed in male mammary tissue both in patients given stilbestrol for prostatic carcinoma and in workers handling stilbestrol (see Hypertrophy of the Male Breast, Chapter 3)

Estrogen is absorbed through intact mucosa and skin and there have been a number of reports (Speert) of its physiological effects upon the breast when administered in the form of an ointment or in some oily alcoholic vehicle All these facts leave no doubt but that estrogen is the chief hormonal stimulant of the mammary epithelium

The remarkable proliferation of the mammary acini during the first half of pregnancy has been explained at least in part as the effect of *progesterone* the corpus luteum hormone Experiments in several laboratories during recent years have proved that in most species of animals progesterone as well as estrogen is necessary for complete development of the mammary gland There is as yet no adequate histological evidence of the effects of progesterone upon the human mammary gland

That estrogen and progesterone are not the only hormones stimulating mammary epithelial growth was proved in 1930 by Corner who produced breast growth in castrated virgin rabbits with injections of pituitary extract. Subsequently in experiments in a number of laboratories it was found that estrogen fails to make the mammary gland grow when administered to hypophysectomized animals of several species. Turner and his associates succeeded in producing mammary growth with an anterior pituitary hormone which they call mammogen. They extracted the hormone from the pituitaries of pregnant cows and have been able to identify two components a duct stimulating fraction and a lobule stimulating fraction This mammogenic hormone has been shown to stimulate the growth of the mammary glands of castrate male guinea pigs, rats, mice, and rabbits The chemical nature of the so-called mammogenic pituitary hormone remains unknown and its exact physiological role remains somewhat controversial

The Cyclical Changes in the Mammary Gland Associated with Menstruation

A considerable proportion of adult women experience a degree of increased tension or enlargement and tenderness of the mammary gland during the days just prior to the onset of menstruation In some women these changes are so marked as to cause a considerable degree of distress With the onset of menstruation the enlargement and tenderness ordinarily disappear after a day or so In some women however these symptoms persist on into the interval phase of the cycle, or indeed, during the whole of the cycle.

Efforts to correlate these physical changes in the mammary glands during the cycle with histological changes in them have produced conflicting reports Rosenberg, for instance, believed that he saw sprouting and budding of the duct epithelium in premenstrual breasts and that following menstruation the newly formed acini disappeared His evidence was based on autopsy material In a

similar study Dieckmann, however, found no evidence at all of budding of the ducts or other signs of epithelial proliferation during the premenstrual phase, but he did note that during this phase the intralobular stroma of the breast was loose, wide-meshed and edematous, and that the lumens of the acini were dilated and the basal layer of their epithelium vacuolated In the interval phase of the cycle the intralobular stroma became compact, the vacuoles disappeared, and the lumens of the acini became smaller or disappeared

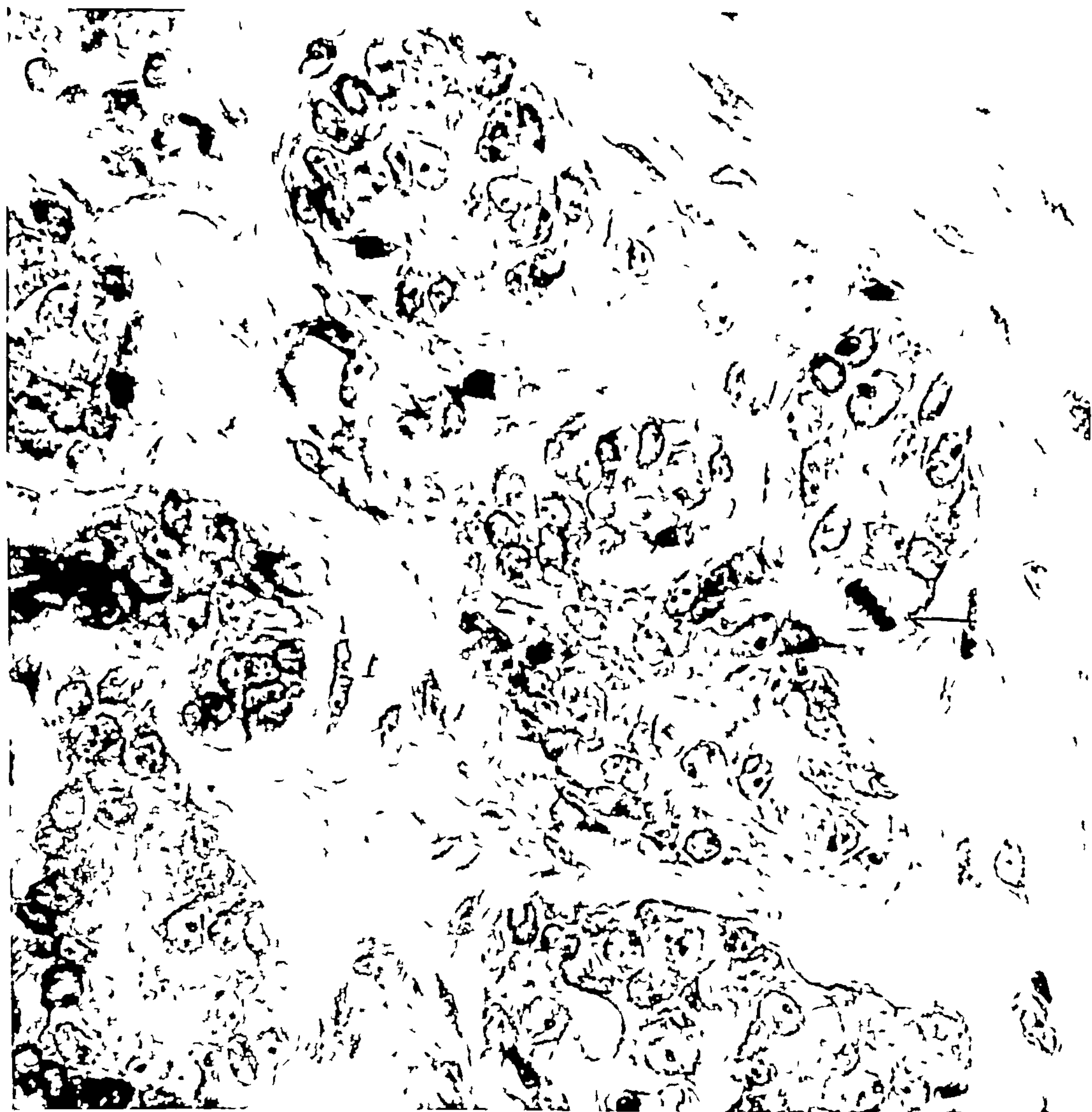


Fig 41 Mitosis in acinar epithelium during the interval phase of the menstrual cycle

In an effort to settle the controversy regarding cyclical epithelial proliferation in the breast, I carried out a histological study of breast tissues removed surgically in the Presbyterian Hospital, correlating the microscopical findings with the stage of the menstrual cycle To determine whether or not there was actual budding of the ducts in the premenstrual phase of the cycle, I counted the numbers of lobules and acini in ten representative fields in each microscopical section The result, shown in Table 5, revealed no statistically significant difference in the different phases of the menstrual cycle Epithelial proliferation, as evidenced by

mitosis and apparent increase in the compactness of the acini was so it seemed to me, seen as often in the interval phase of the cycle (Fig 41) as at any other time

Table 5. Variation in Number of Lobules and Acini According to Phase of Menstrual Cycle

Phase of cycle	Number of cases	Average age	Average number of lobules per low power field	Average number of acini per lobule
Menstrual	23	39 3	5 8	32 0
Interval	59	37 3	6 7	36 2
Premenstrual	18	39 6	7 2	30 2
Total menstruating group	100	38 2	6 6	34 1
Menopause	10	54 8	2 3	11 2

I therefore found no support for the claim that Rosenberg and others have made that there is an increased epithelial proliferation in the breast during the pre menstrual phase of the menstrual cycle

The phenomenon of vacuolization of the basal layer of cells lining the mam mary acini was described by Dieckmann as characteristic of the premenstrual phase of the menstrual cycle I found it present in 33 per cent of the specimens removed during the premenstrual phase in my series of cases It is illustrated in Figure 42 I also found such vacuolization in 12 per cent of my specimens from the interval phase Its significance remains questionable

Edema of the mammary lobule is another phenomenon which was thought by Dieckmann by Moschowitz, and by others to be characteristic of the premen strual phase of the cycle Such intralobular edema is shown in Figure 43 in a specimen from the menstrual phase of the cycle By contrast, Figure 44 shows a large and active appearing mammary lobule without edema in a specimen from the interval phase of the cycle In my data, however intralobular edema was found in only 28 per cent of the specimens from patients in the premenstrual phase of the cycle It was also present to some degree in 22 per cent of the speci mens from patients in the interval phase

It has also been claimed that there is increased cellularity of the stroma of the breast, and lymphocytic infiltration of the lobules, during the premenstrual phase of the cycle I was unable to confirm any of these claims

It is of course obvious that the increase in the size and turgidity of the breasts in the premenstrual phase must be due to some physical change in them Since I found no satisfactory evidence of epithelial proliferation edema, or lymphocytic infiltration during the premenstruum it must be presumed that the swelling and turgidity are due to blood or lymph engorgement or to changes in the extra cellular fluid tension These are changes which we could not expect to demon strate microscopically with ordinary microscopical techniques

It is presumed that the hormonal mechanism that controls this monthly cycle of engorgement of the breast is that which controls the uterine cycle, but the exact chemical mechanism remains wholly unknown

Milk Secretion

Riddle and his associates, in 1932, identified an anterior pituitary hormone which stimulates milk secretion They named it *prolactin* The hormone is present

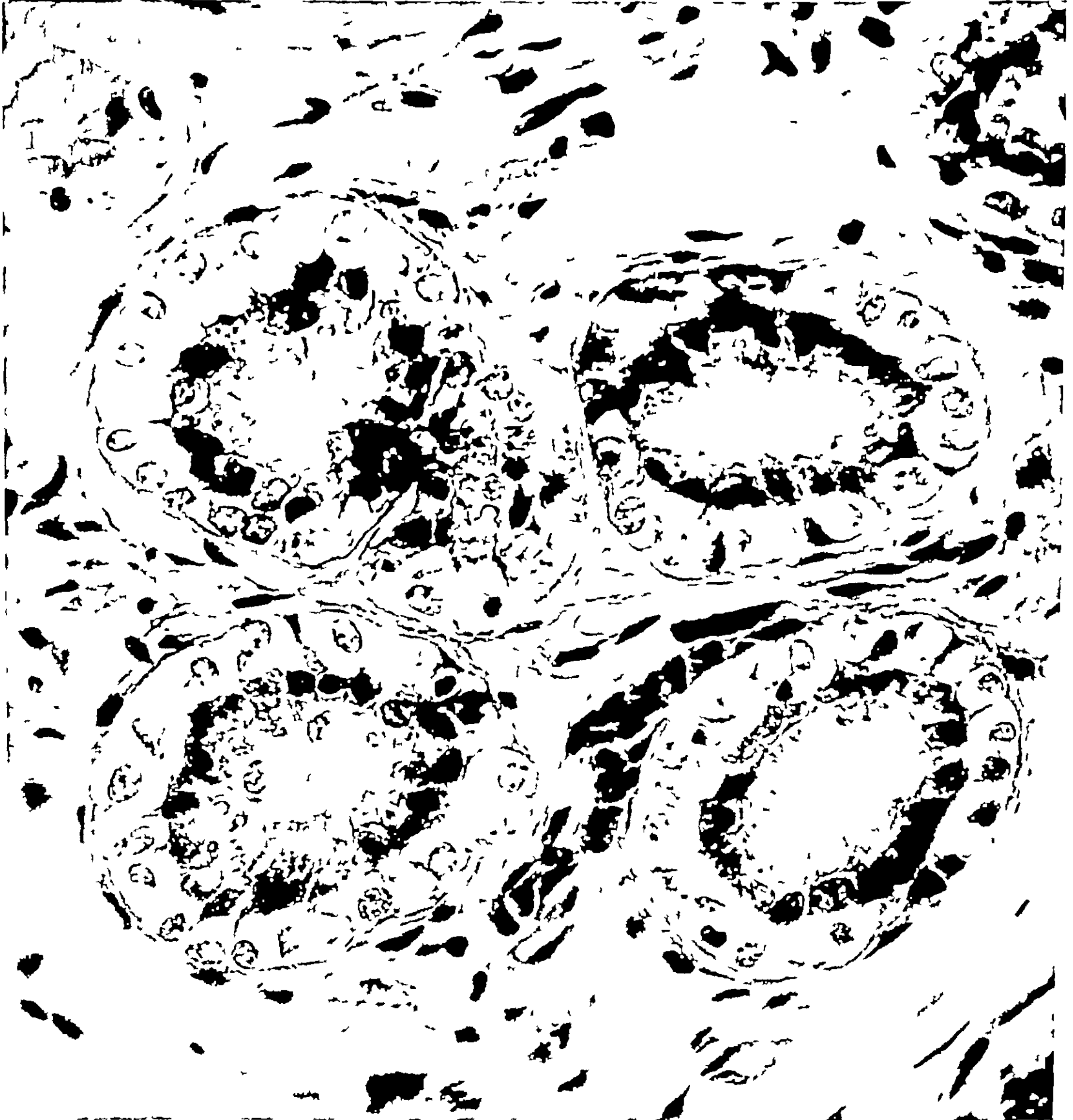


Fig 42 Vacuolization of the cells of the basal layer of the acinar epithelium

in the pituitaries of all vertebrates It is usually extracted from the pituitaries of pregnant cows In the rat, guinea pig, and rabbit, the prolactin content of the pituitary is increased immediately post partum

The actual physiological mechanism by which the mammary gland is suddenly stimulated to produce milk after delivery still remains unknown It has been suggested that a lactation-inhibiting factor, which is present during pregnancy, prevents the breast from secreting during this period, even though it goes through the stage of intensive proliferation preparatory to lactation Some evidence

Fig 43 Intralobular edema in menstrual phase of cycle.

Fig 44 Mammary lobule showing no edema—interval phase of menstrual cycle

suggests that this lactation inhibitor is progestin The idea that estrogen is the inhibitor has found more support recently

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CHAPTER 3

HYPERTROPHY OF THE BREAST

The mammary glands in both sexes may enlarge abnormally at any age, merely as the result of an abnormal physiological stimulus causing overgrowth and not on account of neoplastic changes in the breast itself These physiological hyper trophies are often obscure in nature, and consequently difficult to classify

Hypertrophy of the Female Breast

Precocious Development of the Breasts In female children the breasts may begin to develop very early as part of the syndrome of precocious puberty Most gynecologists consider puberty precocious when it begins before the age of 9 with an arbitrary lower limit of 8 years Yet there are occasional children in whom the first signs of puberty appear within the first two or three years of life These signs are in most instances growth of the breasts and the appearance of pubic hair Growth of the labia and menstruation develop later

Because of our new knowledge of the dramatic endocrine effects of granulosa cell and other ovarian tumors it has been the fashion to suspect the presence of an ovarian tumor in a child in whom puberty is precocious Novak has quite properly emphasized however that in most cases of precocious puberty no demonstrable causative lesion is ever found In this idiopathic or constitutional type of precocious puberty as Novak calls it, the child develops perfectly normal puberal phenomena at an abnormally early age During the subsequent life of these patients no etiological factor explaining their precocity is ever found Their adolescence although premature is normal

Novak s designation the *constitutional type* for this type of precocious puberty is an apt one because not only the genital system but the skeleton matures precociously The children appear to grow with abnormal rapidity and are tall for their age They not only menstruate unusually early but they also ovulate It seems improbable that mere estrogen production such as might be due to the presence of a granulosa cell ovarian tumor could account for this complex precocious growth mechanism

Studies of the excretion of sex hormones in these precocious children (Nathan son and Aub Talbot et al) have shown that there is an elevation of the excretion of gonadotropins estrogens and 17 ketosteroids which approaches adult levels

The hypertrophy of the breasts, which marks the onset of the genital development in the constitutional type of precocity may be noted at an astonishingly early age In Case No 1 of Novak s series it was noted at 6 months of age Menstruation began at 15 months The child was normal except for her pre

cocity, at 10 years of age In Novak's Case No 5 breast enlargement began at 2-3/12 years, and in his Case No 8 at the age of 2 years

The constitutional type of precocious puberty is much more frequent, according to Novak, than precocity due to granulosa cell ovarian tumor He reported six examples of the former type occurring in his own practice, but of the three examples of the latter type which he described none occurred in his own practice This preponderance of the constitutional type has also been observed in the Babies' Hospital, from the records of which the following example of this condition has been chosen



A B

Fig 45 Breast hypertrophy in constitutional type of precocious puberty *A*, 2-7/12 years *B*, 7-4/12 years

R H was admitted to the Babies' Hospital as a patient of Dr Rustin McIntosh, on 9/27/43 She was then 2-7/12 years of age Three months previously her mother had noted that she was growing abnormally fast and that her breasts were enlarging and that some pubic hair had developed

Examination showed the child to be within the range of normal for all body measurements except height, in which she was grossly above normal There was noticeable growth of dark hair over her back and limbs The breasts showed beginning development with definite palpable glandular tissue and well defined areolae and nipples (Fig 45*A*) A vaginal smear showed cells of the postpuberal type The labia were enlarged

but the clitoris was normal Skeletal films showed the skeletal age to be approximately 5 years. Urinary 17 ketosteroids totalled 0 9 mg in twenty four hours

Her accelerated skeletal growth and her precocious sexual development continued during the following five years of observation She menstruated first at the age of 6-10/12 years. At the age of 7 she was found to have diabetes which was controlled with insulin. At 7-4/12 years she weighed 74½ lbs and was 57½ inches in height Her breasts and external genitalia (Fig 45*B*) resembled those of normal puberty

At no time was there any evidence of ovarian adrenal or cerebral neoplasm

Enlargement of the breasts in female children has in rare instances been associated with ovarian tumors I have already referred to Novak s report of three cases in which such breast enlargement was part of a syndrome of precocious puberty caused by a granulosa cell tumor

Lutein cysts of the ovary have also caused precocious development The following is an example of this process from the service of Dr Edward J Donovan in the Babies Hospital

C. C aged 3 years was admitted April 30 1934 One month previously the mother noted that the child s abdomen was enlarging and that her breasts were also abnormally prominent.

Examination showed the abdomen to be greatly enlarged due to the presence of a soft, freely movable tumor The breasts were enlarged the mass of glandular tissue in each being about the size of a walnut (Fig 46) There were no other apparent abnormalities.

At laparotomy a cyst 14 cm. in diameter arising from the left ovary was found It weighed 260 gms. It was filled with blood-stained fluid The wall varied from 3 to 9 mm. in thickness, and from its thickest part a few low papillary ingrowths projected into the interior Microscopic study showed it to be a lutein cyst. The child developed a wound infection followed by pneumonia and empyema and finally died

Microscopical study of the hypertrophied breasts showed little evidence of epithelial proliferation The number of ducts was somewhat increased but there was no acinar development

Lesions of the third ventricle and tumors of the adrenal cortex are rare causes of precocious hypertrophy of the female breast

Another type of abnormal development of the breasts is that in which the mammary gland begins to develop at the age of nine or ten years This is not by definition of the gynecologists precocious, but merely early development. A discoid, soft mass of tissue from 3 to 6 cm in diameter develops beneath the nipple This phenomenon is often unilateral and causes the family and some physicians to fear that a neoplasm is present Biopsy and even excision, has often been performed I cannot condemn too strongly any kind of surgical procedure under these circumstances It is very apt to interfere with the subsequent normal development of the breast The only kind of treatment that is needed for this kind of a tumor of the breast is reassurance and patience Within a few months the opposite breast will show a similar development. Neoplasms of the mammary gland at this age are so rare and the hazard of biopsy of the abnormally early developing breast is so great, that the wisest course is to do nothing

Adolescent Hypertrophy The most frequent type of true hypertrophy of the female breast is that which occurs during adolescence following normal puberty The breasts instead of ceasing to enlarge when they have reached normal limits

continue to grow Over a period of a year or two of excessive growth the breasts may become so large that they are a great physical and psychological burden to the unfortunate girl The abnormal drag of breast weight upon the shoulders in the erect position may cause so much distress that these patients are comfortable only when lying down

The individuals thus affected may have a comparatively normal menstrual history, but in several of the patients whom we have studied a degree of endocrine abnormality was suggested by low fertility

When this adolescent type of breast hypertrophy develops, the breasts do not regress in size with maturing years The patient has no hope of spontaneous relief from her burden

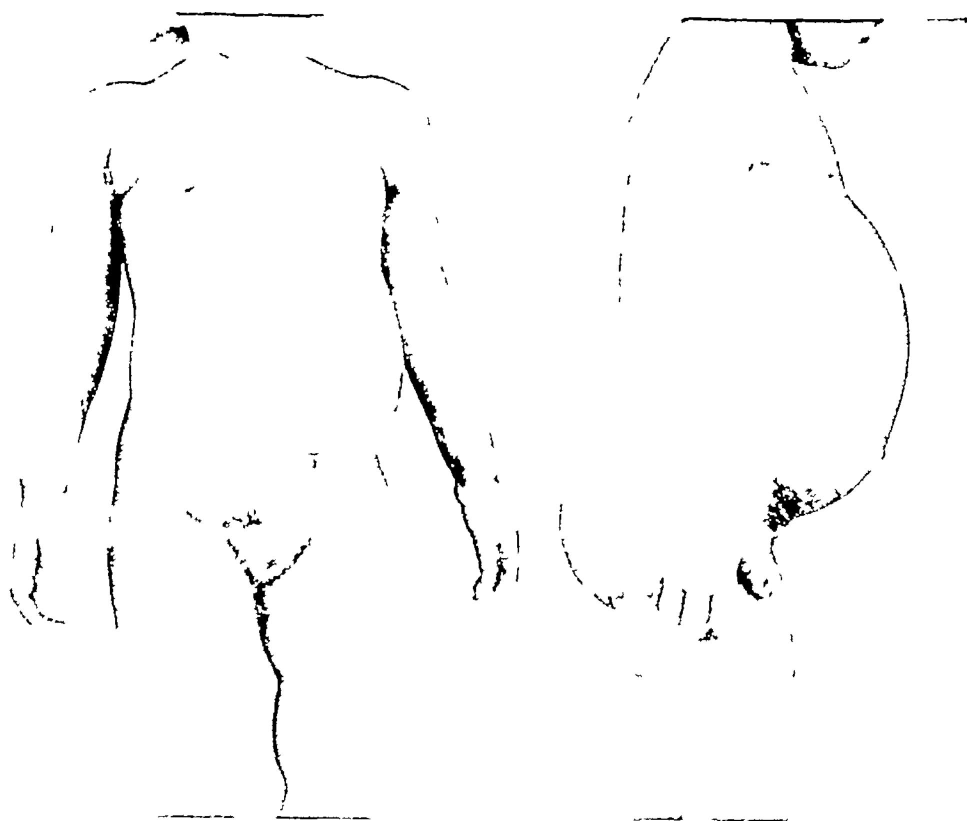


Fig 46 Hypertrophy of breasts due to lutein cyst Age 3 years

The following is a typical example of the adolescent type of breast hypertrophy

F J came to the Presbyterian Hospital at the age of 30 for relief of hypertrophy of her breasts, present since puberty Her breasts had begun to develop at the age of 12, and efforts were first made to restrain their growth by applying a tight binder They continued to grow rapidly, however, and soon reached an abnormally large size This persisted up to the date of her admission (Fig 47) Her breasts hung to below the level of her umbilicus, and dragged so heavily that she attempted to support them by means of a special bag-like brassiere

The adolescent type of hypertrophy sometimes affects one breast much more than it does the other This is difficult to explain on an endocrine basis, for one

would assume that the hormonal growth stimuli carried by the blood stream would reach both breasts in equal amount

The following is an example of asymmetrical adolescent breast hypertrophy

H S came to the Presbyterian Hospital at the age of 19 complaining of hypertrophy of the left breast. At the age of 14 her left breast began to increase in size out of all proportion to her right breast which developed normally with the onset of normal

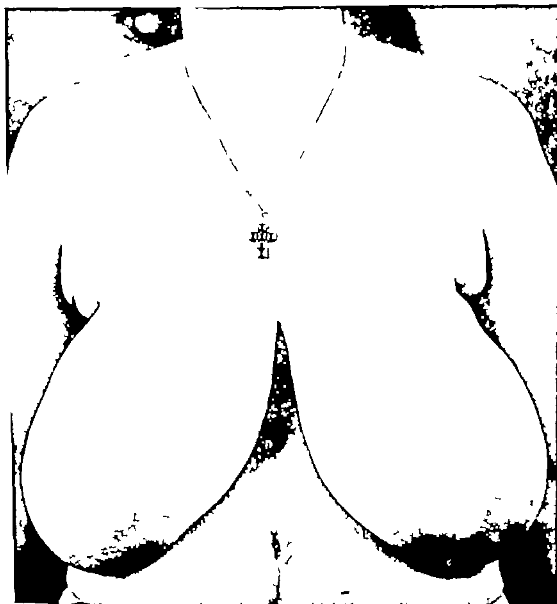


Fig 47 Adolescent type of hypertrophy of breasts.

menses at the age of 14½ During the eighteen months preceding her admission to the hospital, the rate of enlargement of the left breast had increased

Examination showed a normally developed young woman except for a greatly hypertrophied and dependent left breast (Fig 48) The right breast was normal A plastic resection of part of the hypertrophied breast was performed.

Microscopic study of this type of adolescent hypertrophy of the female breast shows surprisingly little that can be termed abnormal The epithelial elements are not remarkable The excessive growth appears to be on the part of the connec

tive tissue and fat The relative proportions of these elements in any particular example of breast tissue are difficult to assess from microscopical study Figure 49 shows a typical example of adolescent hypertrophy

Hypertrophy of the Male Breast

In males the breasts occasionally show transient hypertrophy at two ages, at puberty, and in the sixth or seventh decades of life For lack of better terms I



Fig 48 Asymmetrical adolescent hypertrophy of breasts

have called the lesion in youth *puberal hypertrophy*, and that in old age *senescent hypertrophy*

Puberal Hypertrophy A large proportion of boys between the ages of 13 and 17 show a slight degree of mammary gland enlargement which is transient and passes unnoticed In occasional subjects the hypertrophy is more marked It consists of a circumscribed discoid enlargement of the mammary gland directly beneath the areola, measuring 2 or 3 cm in diameter It is usually somewhat

tender In most subjects such hypertrophy is bilateral but it is sometimes limited to one breast

Microscopically growth of ducts without the development of gland fields is seen The lining epithelium of the ducts sometimes shows low papillary proliferation The bulk of the lesion however is formed by an increase in the fibrous stroma Karsner has described the histology of these lesions in detail

This form of puberal hypertrophy disappears spontaneously after a few months Jung and Shafton have emphasized that the phenomenon is a normal physiological response to the hormonal stimulus of puberty and that if searched for it will be found with a considerable frequency No treatment other than reassurance is required It is certainly unjustified to excise these puberal hyper



Fig. 49 Microscopical appearance of adolescent type of hypertrophy of female breast.

trophic breasts without waiting at least a year for the normally expected regression of the hypertrophy to occur

Nathanson (1942) studied the excretion rates of estrogens and 17 ketosteroids in puberal hypertrophy and found them atypical He suggests that the phenomenon is due to an hormonal imbalance with estrogen playing the more important part We have not been able to confirm Nathanson s laboratory findings. In a number of our patients with this type of mammary hypertrophy urinary estrogen and 17 ketosteroids have been within normal limits.

In rare instances puberal hypertrophy progresses in one breast to a stage where the organ resembles on a small scale, its female counterpart and the expected regression does not occur Surgical excision is then justified and should be done through a circumareolar incision in order to avoid a visible scar The following case illustrates this condition

M K., aged 18 came to the Presbyterian Hospital complaining of enlargement of the right breast. The enlargement had developed four years previously at the age

of 14, and had persisted without undergoing any change On examination the right breast resembled a small adolescent female breast with a well defined areola and nipple (Fig 50) The left breast was normal In all other respects the boy was normal His external genitalia were well developed, and he had more chest hair than most males

'On 6/17/50 Dr Jerome Webster, whose patient he was, excised the breast Microscopical study showed the breast to consist for the most part of a dense fibrous stroma. he only epithelial elements were scattered ducts without accompanying acini (Fig 51)

Senescent Hypertrophy. Older men, usually between the ages of 50 and 70, occasionally develop hypertrophy of the breasts which is similar to that occurring

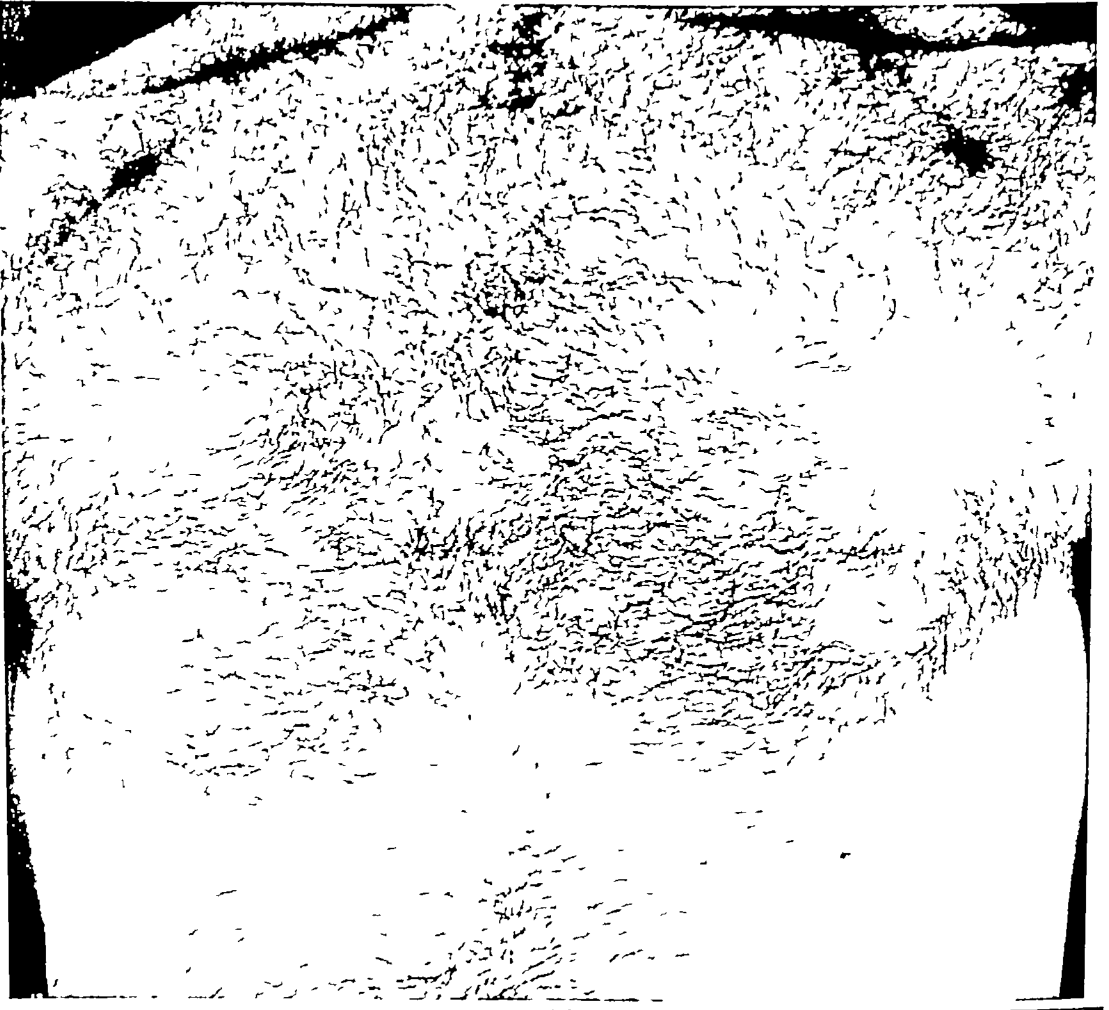


Fig 50 Persistent puberal hypertrophy of the right breast

in boys at adolescence The hypertrophy, which is not infrequently unilateral at first, with the opposite breast being affected later on or to a lesser degree, takes the form of a tender discoid tumor beneath the areola It is usually from 2 to 4 cm in diameter

Microscopically this senescent hypertrophy resembles the puberal hypertrophy of youth The bulk of the lesion is made up of fat and fibrous stroma Scattered ducts, without acini, are seen

This lesion, because it occurs in the cancer age, has to be differentiated from carcinoma Its tenderness and the bilateral involvement, if it is present, are,

of course, important points in favor of hypertrophy Hypertrophy tends to be more circumscribed than carcinoma and it is not accompanied by the abnormal skin attachment which is usually evident in carcinoma But judgment concerning these features requires a good deal of clinical experience If doubt remains as to the nature of the process biopsy should be done

The senescent type of mammary hypertrophy usually regresses spontaneously within six to twelve months If the diagnosis is reasonably certain no treatment is required other than observation at monthly intervals until the hypertrophy regresses

This transitory mammary hypertrophy of older men must be regarded as a kind of physiological aberration not associated with any recognizable endocrine

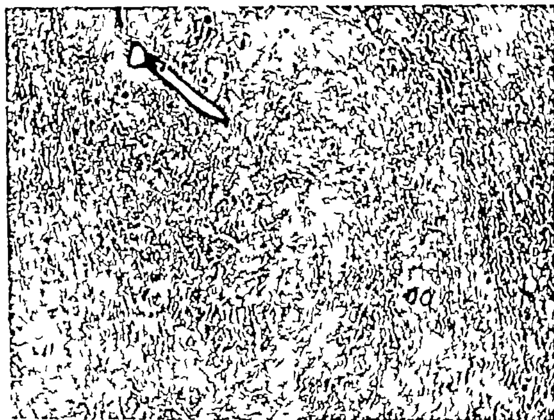


Fig 51 Microscopical appearance of puberal hypertrophy of male breast.

abnormality Nathanson (1947) in excretion studies of these patients, found the 17 ketosteroids and the gonadotrophic titer at normal levels for older males. Our own experience confirms these findings

Hypertrophy Associated With Organic Disease Hypertrophy of the male breast occurs, more often than is generally appreciated, in association with organic disease elsewhere in the body Some of these forms of gynecomastia follow

1 One of the diseases in which a slight degree of hypertrophy of the breasts is occasionally seen is hyperthyroidism Starr described and illustrated such cases

2. In Addison s disease hypertrophy of the breast is sometimes seen according to Robert F Loeb Treatment with desoxycorticosterone may induce gynecomastia if it was not present before The hypertrophy may affect only one breast.

3 Cirrhosis of the liver is occasionally accompanied by gynecomastia (Edmondson, Glass, and Soll)

4 Gynecomastia develops with embryonal carcinoma, seminoma, chorionepithelioma (Gilbert), as well as with interstitial cell tumors (Hunt and Budd) of the testis The degree of hypertrophy of the breasts seen in chorionepithelioma may be very great, so much so that they come to resemble those of a female

Extensive hormonal secretion studies have been made in patients with these testicular tumors (Twombly, Hamburger) Zondek made the original observation that there is a striking increase of an gonadotrophic anterior pituitary-like hormone in the urine In some patients there is also an abnormal estrogen excretion

These hormone determinations have been used as a means of detecting the continued persistence of the disease and for determining prognosis It is generally agreed that the occurrence of gynecomastia in a patient with a testicular tumor, reflecting as it does the elevation of gonadatropin and estrogen, is a bad prognostic sign

5 Adrenal cortical tumors in males may produce feminization with gynecomastia Increased excretion of both estrogen and 17-ketosteroids has been reported with these tumors They are exceedingly rare, but Wilkins has been able to collect reports of 11 such feminizing adrenal tumors in adult males He also described a case in which this type of tumor caused hypertrophy of the breasts in a 5 year old boy

6 An idiopathic type of testicular atrophy, described by Klinefelter, Reifenstein and Albright, is associated with gynecomastia The breast enlargement in this disease is always bilateral and of considerable degree The genitalia are normal except for the small size of the testicles Aspermatogenesis and an increased pituitary follicle-stimulating hormone excretion in the urine are regularly found

7 Weber and other German authors have described a form of gynecomastia, occurring in males of all ages, and characterized by proliferation of both the fibrous and epithelial elements of the breast, which they attribute to the inadequate nutrition during the post-war years in Germany

Klatskin and his associates reported a group of 48 such cases of gynecomastia occurring among 300 American soldiers who, as prisoners of war in Japanese prison camps, suffered severe malnutrition The urinary 17-ketosteroids were found to be significantly lowered in the patients with gynecomastia as compared with normal individuals from military or civilian populations

Hypertrophy Associated with Genital Abnormalities. Marked hypertrophy of the male breast has been observed in association with abnormalities of the male genital tract Three such cases from the records of the Presbyterian Hospital are summarized below

Case 1. W S , came to the Presbyterian Hospital at the age of 33, because of hypertrophy of the breasts This had first been noted when he was 13 years of age, and had gradually increased during subsequent years On admission he presented the typical picture of eunuchism He weighed 260 pounds His penis measured only 3 cm in length and no testes were palpable The breasts were markedly enlarged, particularly the right one which was at least the size of a normal adult female breast The left breast was about half as large Both had well developed areolae and nipples (Fig 52)

On 3/30/43 Dr Jerome Webster whose patient he was, performed bilateral mastectomy through circumareolar incisions. Microscopic study showed that the hypertrophic breast consisted largely of fat and fibrous tissue. No gland fields were seen and only a few scattered ducts

Case 2 C. F aged 12 years, came to the Presbyterian Hospital for the repair of a complete hypospadias with which he had been born The external genitalia were otherwise normal. The hypospadias was repaired in stages and was completed at the age of 15 At the age of 13 his breasts began to enlarge. They were not tender The



Fig 52. Hypertrophy of male breasts associated with eunuchism.

enlargement continued until at the age of 16 they resembled the breasts of a female of similar age (Fig 53) They were quite symmetrical The areolae and nipples were well developed

When the boy was 17 Dr Jerome Webster whose patient he was, performed bilateral mastectomy through a semicircular intra-areolar incision. Microscopical study (Fig 54) showed proliferation of ducts, with slight papillary heaping up of the lining epithelium in some. No acini were seen. The bulk of the hypertrophic tissue was fibrous stroma

Case 3. M P, aged 34, came to the Presbyterian Hospital because of sterility At the age of 4 he had had mumps At the age of 18 it became apparent that he was undeveloped sexually, and during the following years he was given antuitrin S and testosterone in varying amounts without much change in his eunuchoid physique He married at the age of 29 but remained sterile

Examination on admission showed that the patient was still a typical eunuchoid He was tall, slightly obese, with broad hips, smooth skin and no facial hair His pubic hair was scanty and had a female distribution His testes were descended but small, and his penis normal in size There was moderate hypertrophy of both breasts, including nipples and areolae



Fig 53 Hypertrophy of male breasts occurring with hypospadias

The patient was given increased amounts of testosterone Three years later, in 1949, an occasional drop of bloody discharge was noted from the left nipple for the first time By the following year a similar brownish discharge appeared from the right nipple The breasts meanwhile had not changed in character

On 3/31/50 bilateral mastectomy was carried out through circumareolar incisions The terminal ducts beneath the nipples were grossly dilated and filled with brownish fluid Microscopically the breasts showed dilated ducts with some papillary epithelial proliferation of the apocrine type, but no acini (Fig 55) The dilated ducts had thickened walls and showed some periductal lymphocytic infiltration, giving a picture reminiscent of ectasia in the female breast



Fig. 54 Microscopical appearance of hypertrophy of male breast occurring with hypospadias.



Fig 55 Dilated ducts in male breast following androgen treatment

Fig 56 Idiopathic hypertrophy of breast in boy aged 8

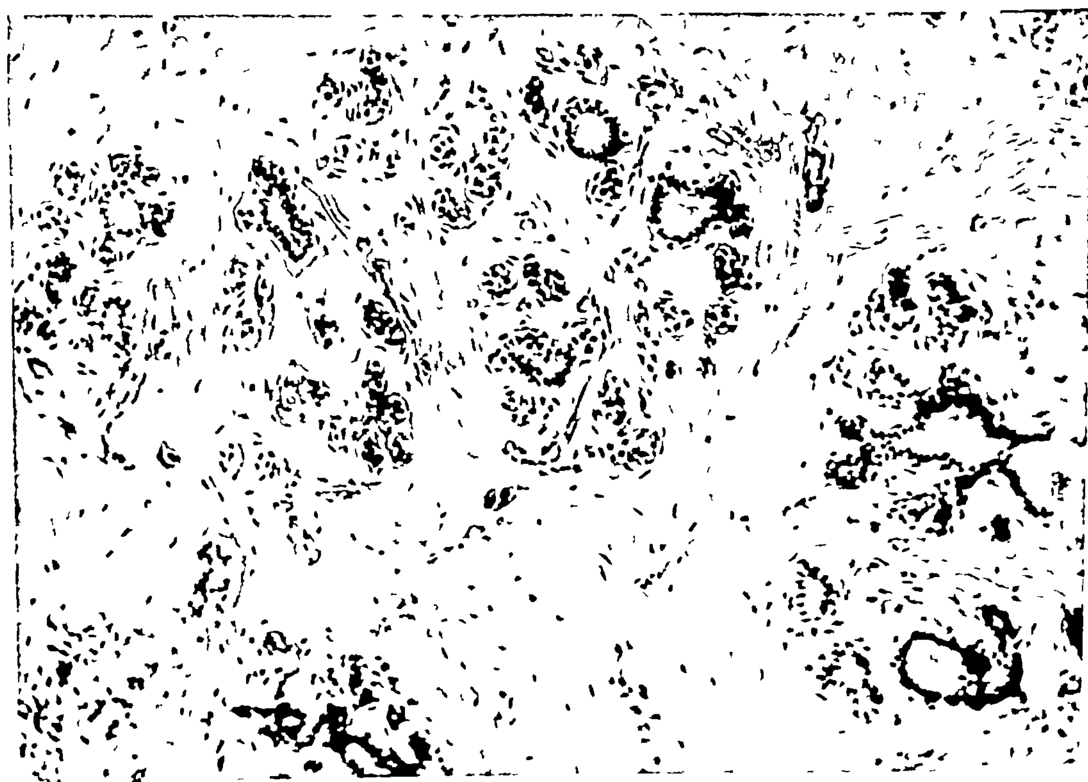


Fig 57 Microscopical appearance of idiopathic hypertrophy of breast in boy aged 8

Three years postoperatively the bilateral brownish nipple discharge reappeared I assumed that the breasts had not been entirely removed (the circumareolar incisions which were utilized making complete removal of the comparatively extensive breast tissue impossible) and that the same process of epithelial stimulation as the result of long continued androgen administration *was now again producing bloody nipple discharge.*

Idiopathic Hypertrophy In contrast to these cases of hypertrophy of the male breast associated with abnormalities of the genital tract there are other cases in which hypertrophy develops at an early age and persists, without any

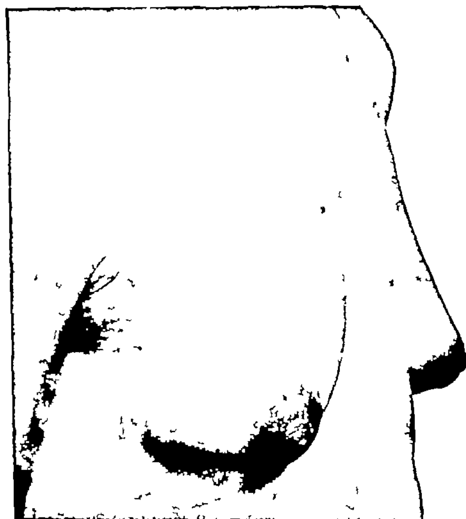


Fig 58 Bilateral hypertrophy of male mammary gland resulting from administration of 500 mg of diethylstilbestrol daily for one year for carcinoma of the prostate.

evidence of associated abnormality of the genital tract, or organic disease elsewhere The following case illustrates this type of lesion

R. R., aged 8 was brought to the Presbyterian Hospital because of swelling of the right breast. This had first been noted at the age of 6½ years and slowly increased over a period of a year and a half Examination showed the left breast to be uniformly enlarged. It measured 6 x 4 x 3 cm., and resembled the breast of a female at the beginning of adolescence The areola and nipple were well developed, *in keeping with the* breast hypertrophy The right breast was undeveloped as in a normal preadolescent boy (Fig. 56) There were no other signs of endocrine abnormality The external genitalia were normal.

Fig 56 Idiopathic hypertrophy of breast in boy aged 8

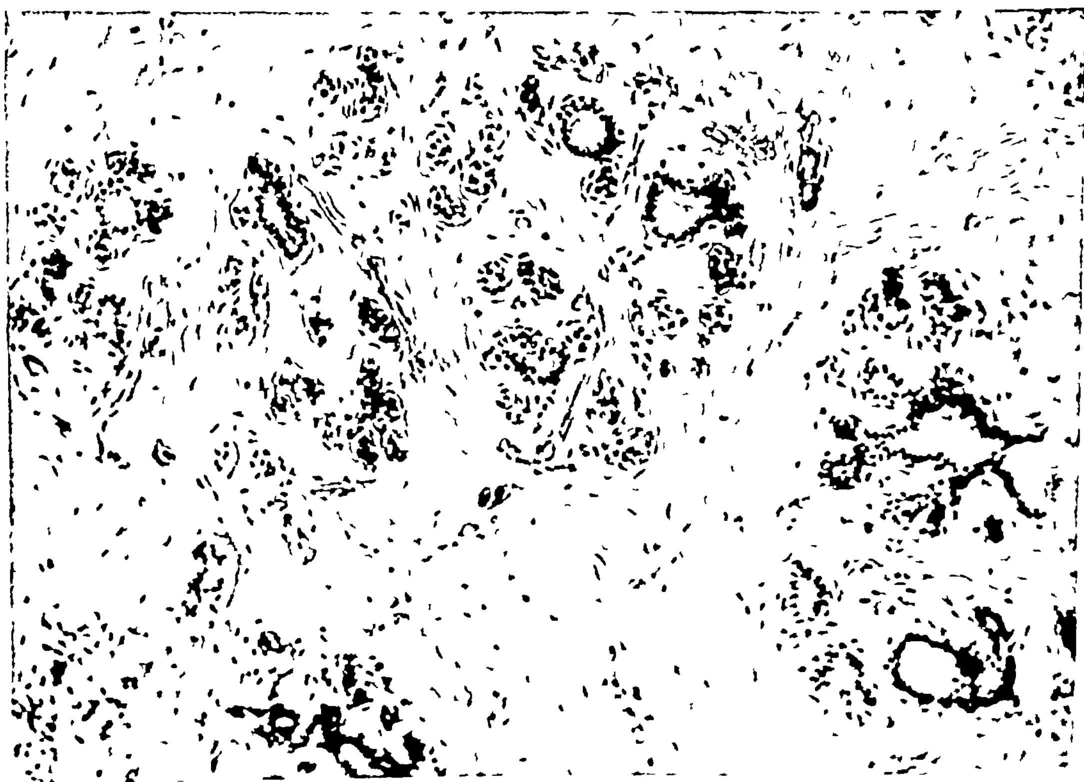


Fig 57 Microscopical appearance of idiopathic hypertrophy of breast in boy aged 8.

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After following the boy for two years, during which regression of the hypertrophied breast did not occur, Dr Jerome Webster, whose patient he was, excised the left breast through a circumareolar incision, on 8/8/51

The microscopical sections showed extensive growth of acini around terminal ducts, to form small gland fields, giving the picture of active epithelial proliferation (Fig 57)

This form of gynecomastia differs from the others that I have described in that the breasts show proliferation of acinar as well as duct elements The stimulation to breast growth, whatever its origin, is therefore a complete one, resembling that in the pubescent female

Hypertrophy of Breast Produced by Androgen and Estrogen. Both estrogen and androgen given therapeutically will cause hypertrophy of the male breast It may seem paradoxical that these opposing hormones produce a similar clinical effect, but it is a fact

Breast hypertrophy is commonly seen in men who are given stilbestrol therapeutically for carcinoma of the prostate, or for other disease Figure 58 shows the breast enlargement in such a patient Moore and his associates wrote a good description of the microscopical changes in the mammary glands in these patients There is marked increase of the stroma with multiplication of ducts and proliferation of their lining epithelium There is some degree of budding of the ducts, but fully developed gland fields are not seen Similar hypertrophy of the male breast has been reported in workers engaged in the manufacture of stilbestrol (Scarff and Smith, Finkler, Fitzsimons)

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Table 6. Can Cancer be Cured? (Paterson and Aitkin Swan Survey)

Yes usually / sometimes / seldom		36%
No never		50%
Do not know		14%
Sample	1200	

Table 7 Do You Think Cancer is Curable (American Institute of Public Opinion Surveys)

	1940	1950	1953
Yes	56%	60%	65%
No	27%	23%	20%
Do not know	17%	17%	15%

Self Examination

Having taught women that it is of vital importance to find disease in the breast at an early stage of its evolution our next duty must be to teach them how to do so To those who object to women taking an active part in the detection of their own breast disease rather than leaving the problem to physicians I can only point out that, even if all physicians were ideally trained and able to detect breast carcinoma in its earliest palpable stage the proportion of breast carcinomas discovered in this way would be relatively small, because only a small proportion of all adult women present themselves for physical examination often enough to assure the diagnosis of breast carcinoma at an early stage In order to be reasonably certain of detecting breast carcinoma at an *early stage* the breast must, I believe, be examined at least every two or three months. There are not enough physicians, enough time, or enough money to achieve this, even if women could be persuaded of the desirability of consulting physicians every two months for physical examination Recent data collected by the American Institute of Public Opinion have shown that only about one-third of the women questioned in a survey of medical care had consulted a physician within two months

I see no escape from the simple fact that if breast disease is to be detected at an earlier stage in its development, it is the women themselves who must be taught to do it. This fact has led me to advocate the concept of self-examination of the breast. When at first I realized the desirability of self-examination I hesitated to recommend it, being doubtful of the ability of women to detect their own breast disease by self-examination and fearful that the effort to do so would induce cancerphobia As the years have gone by my own experience has reassured me on both counts, and I am today firmly convinced that teaching women to examine their own breasts is the best hope of improving the control of breast disease

Breast disease in general indicates its presence by a tumor A spontaneous nipple discharge is also of course, a sign of disease of some sort but it is a relatively infrequent symptom. Retraction signs, while often present are rarely perceived by the patient herself unless they are very marked Retraction signs therefore are not of much importance in the problem of self-detection of

CHAPTER 4

THE DETECTION OF BREAST DISEASE

Until very recently our attempt to control disease in the breast, particularly cancer, has concentrated upon diagnosis and treatment There has been no organized effort to discover disease at an early stage, even though it is obvious that refinements of methods of diagnosis and treatment can make only a very limited gain in the control of the disease unless it is detected early in its evolution. Breast carcinoma is easily curable by good surgery when the primary lesion is small and only one or two axillary nodes are involved, but when axillary metastases of considerable extent are present, the cure rate is greatly diminished, and when distant metastases have developed, no cures at all are obtained For patients in this last category, improvement in surgical technique offers no hope whatever, because the disease is far beyond the surgeon's reach It has been recognized too late It is high time that we turn our attention to the problem of the early detection of breast disease

Women's Role in the Detection of Their Breast Disease

In the detection of breast disease, both the patient herself and physicians have a role to play I wish first to discuss the patient's share in the responsibility for detection of her disease In educating women for this responsibility, the first step is to convince them that it is worth their while to detect disease in the breast, for, unless women are convinced that cancer of the breast can be cured, it is unreasonable to expect them to make an effort to detect it While we have had a general impression of the fear that the average woman has of cancer of the breast and of her pessimism regarding its treatment, it is only recently that special studies of this question have been made A survey carried out by Paterson and Aitkin-Swan in Manchester, England, in 1953, showed that only 36 per cent of women believed that cancer can be cured (Table 6) There has been very little in the way of public education regarding cancer in Britain In the United States the intensive educational efforts of the American Cancer Society during recent years are perhaps beginning to have some effect upon the attitude of our people regarding the curability of cancer Surveys conducted by the American Institute of Public Opinion (Table 7) show that whereas in 1940 only 56 per cent of people believed that cancer was curable, in 1953 65 per cent believed it to be curable Certainly, educational efforts to persuade women that it is worth while to detect disease in the breast must be continued

diameter At this stage the likelihood of metastasis is small The average diameter of breast carcinomas coming to the Presbyterian Hospital however has been 5 1 cm and more than 60 per cent of the patients have had axillary metastases The chance of cure is closely dependent upon the frequency of axillary metastasis If we could teach women to find their own breast lumps while they are still small it would be the greatest advance toward the control of breast carcinoma that has yet been made

The Technique of Self Examination

It is of great advantage to a woman in examining her own breasts just as it is to a physician making such an examination to use a correct and thorough technique It seemed to me that self-examination could be taught best by a motion picture film In 1949 I went to the officials of the National Cancer Institute of the United States Public Health Service and of the American Cancer Society and persuaded them to cooperate in such a teaching film We made a 16 mm sound film in technicolor I planned the script in cooperation with the American Cancer Society technical staff and myself took the part of the examining physician teaching his patient how to examine her breasts In the film we attempted to convince women that it is possible for them to feel tumors in their own breasts and to demonstrate a precise technique of how to go about it.

The method of self-examination that I have taught my patients and which I presented in the film is based on my own method of examining the breast In self-examination the technique is of course simplified

The first step in self-examination should be careful inspection of the breast before a mirror Women should be reassured about the inequality in the size of the breasts that many of them have, and which they may discover for the first time when they inspect their breasts carefully They should be taught to look for asymmetry of the contours of the breasts and dimpling of the skin as well as for flattening, *broadening, and retraction of the nipples They should be taught that* any erosion of the nipple surface no matter how minute, as well as any spontaneous serous or bloody discharge from the nipple (except that occurring during pregnancy) is an indubitable sign of breast disease requiring medical consultation

The second step in self-examination should be to lie supine on a bed or couch The arm on the side to be first examined should be raised above the head and a small pillow or if that is not available a folded bath towel, placed under the shoulder (Fig 59) This elevates the shoulder and shifts the breast somewhat medially so that it is balanced and flattened out in as thin a layer as possible on the chest wall If the shoulder is not elevated, the breast tends to fall laterally and fold upon itself making palpation of the lateral half difficult (Fig 60) because of its increased thickness

In this supine position, palpation of the inner half of the breast is begun with the flat of the fingers of the opposite hand (Fig 61) The palpation must be gentle, because tactile sensitivity is greatest with very gentle palpation The whole extent of the inner half of the breast is explored the examining hand tracing a series of transverse lines from the nipple line to the sternal edge beginning just below the clavicle and descending to the inframammary fold (Fig 62) The mammary tissue may reach the clavicle above and the sternum medially as a thin

breast disease Breast disease does not in general produce pain, although physiological disturbances in the breast often do so The problem of self-detection of breast disease is therefore centered in the problem of training women to palpate their own breasts and find lumps in them

Women ordinarily find their own breast lumps accidentally, while dressing or bathing In passing a hand over the portion of the breast containing the tumor their attention is caught by the change in consistency and form of the breast Sometimes the lumps are very small when found I have known many that were no more than 1 cm in diameter, yet the woman herself found the lump

The following is such a case history

Mrs X, aged 60, was active in civic affairs, and one day was given a bundle of brochures concerning cancer to distribute to the members of her club She had had no special interest in cancer, and the task had been thrust on her as a duty that a public spirited woman ought to assume As she lay in bed that evening thinking over the day's events, she recalled her promise to distribute the literature, and the fact that she had read none of it herself troubled her conscience So she picked up one of the leaflets and read that a lump in the breast may be a sign of breast cancer As she read, she instinctively put her right hand to the upper outer sector of her left breast She was shocked to feel a very small firm lump She slept badly and the next morning cancelled her plans for the day and consulted her internist He confirmed her finding and sent her to me Her tumor was hard, rather discrete, and measured 10 mm in diameter There was a suggestion of dimpling in the overlying skin There were no palpable axillary lymph nodes At the operation frozen section confirmed the clinical diagnosis of carcinoma Radical mastectomy was done The axillary lymph nodes were not involved All this was 15 years ago, and she is still well It is fair to say that this woman saved her own life by finding her carcinoma at this early stage

If it is possible for women to discover small early carcinomas by fleeting casual palpation of this kind, it is certainly reasonable to expect women to discover tumors earlier if they have been taught to examine their breasts methodically But neither folklore nor education have given the modern woman any idea of the possibility of purposeful self-examination of the breasts The following case history illustrates this fact

Mrs Y, a woman aged 42, while undressing happened to pass her hand over her right breast and discovered a lump in it A paternal aunt had had breast carcinoma She came for examination the following day There was a firm, poorly circumscribed tumor 3 5 cm in diameter in the upper central portion of the breast It was a carcinoma Metastases were already present in the internal mammary lymph node chain She eventually succumbed to the disease She had discovered it too late

This tragedy occurred despite the fact that the patient was the daughter of a physician and the wife of a physician, and as such had a better access than most women to medical knowledge She had had a college education, and following her marriage had taken a prominent part in the Parent Teacher Association work in her community Nowhere in these experiences had she learned that she could guard against breast cancer by examining her breasts herself

The great advantage of finding a breast lump while it is still small is apparent from our data of the natural history of breast carcinoma as presented in Chapter 19 Most breast carcinomas are easily palpable when they are a centimeter in

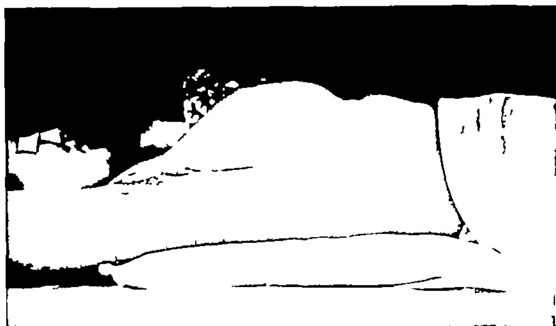


Fig 61 Palpation of the inner half of the breast with the patient's opposite hand

Fig 62 Self-examination of the inner half of the breast shown diagrammatically



Fig 59 Preferred position to begin self-examination of the breast The arm is raised A pillow placed under the shoulder balances the breast upon the chest wall



Fig 60 Incorrect position to begin self-examination of the breast If the patient lies flat, the breast falls to the side

layer, and small breast tumors arising near the breast periphery may seem to be so superficial that they are often mistaken for harmless cutaneous lesions A dominant tumor anywhere in the breast area must be regarded as evidence of disease.

As a part of their instruction in self-examination women should be told of the existence of the inframammary ridge and assured that it is not an indication of disease (see Chapter 5 page 98) Women often mistake this ridge for a tumor Neoplasms do of course sometimes develop within it and stand out as a lump within the ridge.

Having completed her palpation of the inner half of her breast and of its lower edge the woman is ready to examine the outer half of her breast In this

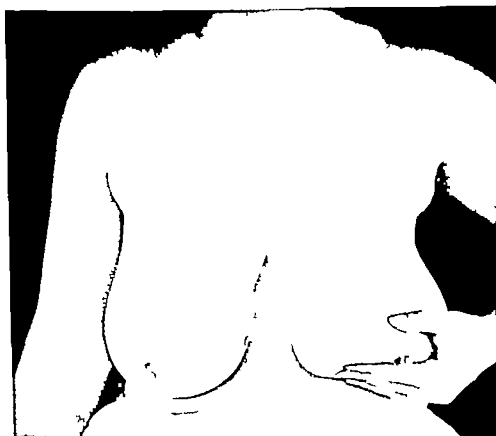


Fig 65 Improper method for self-examination of the breast

step it is preferable to have the arm down at the side in this position the upper outer sector of the breast is more caudad, and therefore more accessible (Fig 63) The examining hand explores the whole extent of the outer half of the breast tracing a series of transverse lines from the nipple line outwards to the posterior axillary line, preferably beginning at the inframammary fold and ascending to the axilla (Fig. 64) The examination ends in the upper outer sector of the breast which is the most difficult to examine because it is the thickest part of the breast This sector more often than any other part of the breast shows nodularity that may be classified as within normal limits It is also the sector in which dominant tumors representing disease are most often found It is the sector of the breast, therefore that should receive the greatest attention in any examination

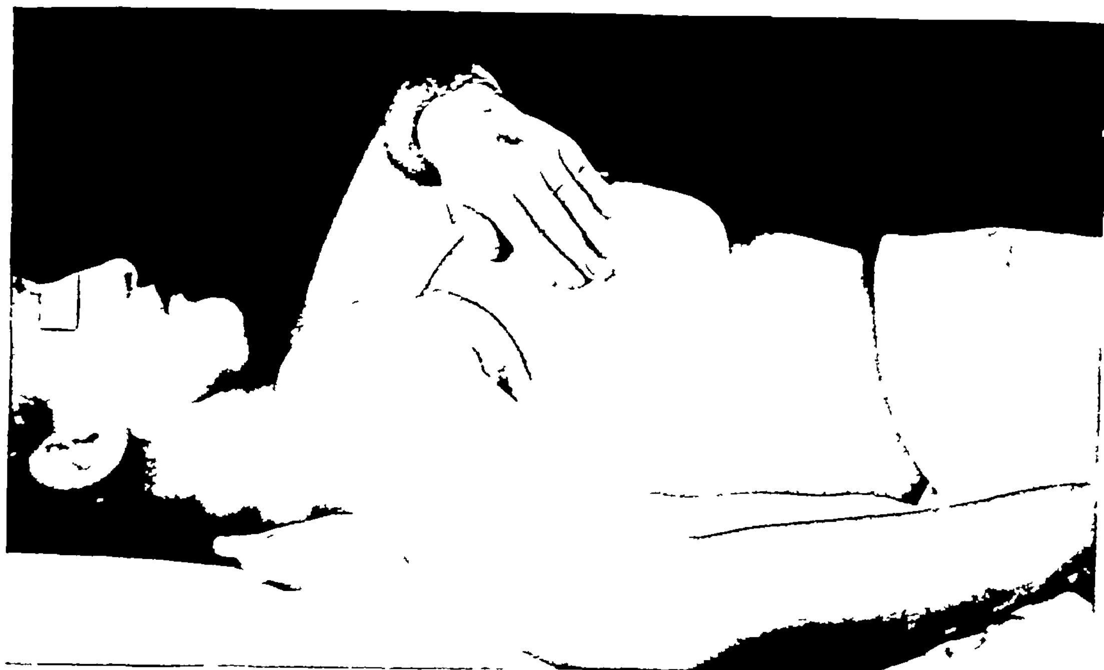


Fig 63 Palpation of the outer half of the breast with the patient's opposite hand The arm is down at the side

Fig 64 Self-examination of the outer half of the breast shown diagrammatically

own families, and the responsibility of parenthood has sobered them and lengthened the shadow of fate before them

The concept of self-examination of the breast is so new that very few data are available as to what success there has been in teaching it. Gowen and his associates have reported that a follow up study of 470 women 18 months after they had been taught my technique of self-examination revealed that 79 per cent of the 129 women who replied to the inquiry were practicing the method, and that as a result one had found a breast carcinoma and eight had found benign tumors

I know from my personal effort in teaching women to examine their own breasts that tumors both benign and malignant may indeed be found as a result of such teaching Not all of the tumors thus discovered have been small but some of those which proved to be malignant have not only been small but had not metastasized The following is a case history

Mrs. Z. aged 42, a physician s daughter attended a showing of the film Breast Self Examination That evening she examined her breasts according to the technique illustrated in the film and found a tumor in the upper outer sector of the left breast. She came at once for consultation. The tumor was firm, poorly circumscribed, measured 2 cm in diameter and gave a definite retraction sign in the overlying skin on forward bending. Radical mastectomy was done Fifty four axillary lymph nodes were found none of which contained metastases

My own experience has convinced me that women can become comparatively expert at palpating tumors in their own breasts They have advantages that an examining physician cannot possess In the first place a woman palpating her own breasts is concerned with the findings in two breasts only As she examines them repeatedly she becomes thoroughly familiar with their special characteristics An examining physician has to attempt to recall the comparative findings in a great many breasts a difficult feat no matter how detailed his written records may be A woman examining her own breasts has a second important advantage it is the proprioceptive tactile sense that helps her in palpating her own tissues

To further emphasize that women may become expert at self-examination of their breasts, I must point out that in several instances women have come to me with small breast tumors which they had discovered but which I was unable to find in my first palpation As a result of such experiences I have learned, in all humility to ask patients in whom I have not found a tumor whether or not they feel one and if they do to show me its location

Teaching women to examine their own breasts will, beyond question, produce cancerphobia in some women and do them more harm than good. There are some women so unstable mentally that fear of cancer often focused by family tragedy due to the disease, makes any rational consideration of it impossible. Some cannot palpate their breasts at all without becoming terrified Others palpate them daily and constantly torment themselves with thought of the disease Physicians should therefore take care to teach self-examination only to those of their patients whom they know well enough to be certain that they will be able to think about the problem with the necessary degree of detachment. When the concept of breast self-examination is presented to women at large by means of the film however there can be no selection of subjects and some harm will certainly result.

I believe that women should be discouraged from palpating their breasts while sitting up (Fig 65) If the breast is of average or larger than average size, palpation is more difficult in the erect position than in the supine position In the erect position the lower dependent half of the breast is folded upon itself, and a small tumor may be masked by this increased thickness

When women adhere to the routine of this technique they become familiar with the physical characteristics of their breasts as revealed by repeated palpation with this one preferred method They are then more likely to identify any small tumor that may develop

In advising as to the frequency with which self-examination should be carried out, we face the dilemma of not wanting women to examine their breasts so often that they develop cancerphobia, but wanting them to carry out the examination often enough so that they have a reasonable chance of detecting carcinoma while it is yet in an early stage My clinical experience with carcinoma of the breast has convinced me that the disease progresses more slowly than is generally thought I believe that it takes at least from 6 to 12 months for a carcinoma to grow from a diameter of about 1 cm , at which it first becomes easily palpable, to 5 1 cm , the mean diameter of carcinomas in women coming for treatment today in the Presbyterian Hospital The aim with self-examination is, of course, to enable women to discover their breast tumors as soon as possible after they become palpable We wish to push the moment at which the tumor is discovered backward in time into the 6 to 12 month period that now elapses between the time a tumor becomes palpable and the time it is actually found It would be preferable, if it did not produce cancerphobia, to advise that self-examination of the breast be carried out at monthly intervals In an effort to guard the patients whom I instruct in self-examination against cancerphobia, I appeal to them not to palpate their breasts at any other occasion than the monthly examination and not to think about breast disease except on this one occasion

For women who have not reached the menopause it is important to choose the correct phase of the menstrual cycle for self-examination of the breasts In a considerable proportion of women there is enough vascular engorgement of the breasts in the premenstrual phase of the cycle to produce slight enlargement and increased turgidity of the breasts, and some tenderness In a smaller number of women the engorgement is sufficiently pronounced to produce a degree of nodular thickening that may deceive the examiner into thinking actual tumors are present It is desirable to carry out self-examination at the time when these transitory physiological changes are at a minimum, namely, in the immediate postmenstrual phase of the cycle

The question of what age is the right one to introduce the subject of self-examination is a debatable one It is ridiculous to attempt to teach it to girls in their teens It is doubtful that even young women in their final college years are mature enough for this discipline It seems reasonable to begin instruction when women are in their early 30's This is the age at which breast carcinoma first begins to have a considerable frequency, and it is the earliest age, in my opinion, at which women are willing to give thought and attention to such a serious subject as the detection of breast carcinoma At this age they have founded their

considerably more frequently in women who have had breast cysts as well as in those who have a family history of the disease as is shown in Chapters 7 and 17 It is particularly worth while therefore to examine the breasts in these women They should be examined every three months to be reasonably certain of detecting carcinoma at an early stage

Another method by which physicians may contribute to the discovery of breast disease is through periodic examinations in so-called cancer detection clinics Only apparently well individuals without symptoms are accepted in such clinics While the idea of special clinics for the detection of cancer may at first thought appeal it has some disadvantages The first of these is that it seems to me unwise to establish special clinics for detecting cancer only rather than all disease Periodic check ups aiming at the detection of disease in general are certainly desirable. This idea is not a new one and has proved its worth Such periodic check ups to find new disease should of course be carried on in every physician s office I do not believe that the methods required to detect cancer can be carried out any better in a cancer detection clinic than in the office of the well trained physician

Another handicap of the cancer detection clinics is the difficulty in staffing them with experienced examiners The work is usually done by young physicians without much clinical experience who are paid on a per diem basis

The final test of the value of cancer detection clinics must be however the number of unsuspected cancers discovered in the apparently well subjects The data so far available on this point as regards breast disease are not very impressive, although breast disease is certainly one of the types of disease most easily discovered by simple physical examination Phillips and Miller report that among 7 767 women examined once at the Cancer Prevention Center of Chicago between 1949 and 1951 a definite breast tumor was found in 129 or 1 7 per cent. Thirty seven of these patients were proved to have benign breast disease, while ten had carcinoma. The incidence of unsuspected breast carcinoma in the series of 7 767 patients was therefore 0 13 per cent Axillary metastases were found in only two of the ten patients with carcinoma—a strikingly low incidence Turtola reported finding one unsuspected breast carcinoma among 1 158 Finnish women whom he examined once Walter and Atkinson found one carcinoma of the breast among 422 English women who volunteered to undergo an examination Because it is a long-term study of the incidence of breast disease in symptomless women the report by Macfarlane and her associates is the most important contribution to the subject that has yet appeared In a group of 537 volunteer women without symptoms referable to the breast, a total of 11,203 biannual breast examinations were made during the 11 year period—1942 to 1952 In the course of these examinations 11 breast carcinomas were found But in every case the volunteer had found the carcinoma in her own breast before routine examination It may perhaps be said that these 11 women found their carcinomas because their experience in having their breasts examined biannually by a physician had taught them how to find breast tumors in their own breasts It could be argued from this experience however that self-examination is a more efficient way of detecting breast disease than examination by a physician Whatever the correct explanation may be for the discovery of the 11 carcinomas in Macfarlane s series an encouraging fact

The film "Breast Self-Examination" has now been shown to some millions of women but it is yet too soon for us to draw any conclusions concerning what effect it has had, if any, upon the early diagnosis of breast disease The United States Public Health Service is attempting to study this question Lewison reports that among 2,358 women interviewed six months after they had seen the film, 80 per cent stated that they examined their breasts occasionally in the manner taught in the film, while 33 per cent examined them monthly

In the last analysis the value of the concept of self-examination of the breasts will be determined only by teaching it widely over a long period of time and with the best modern educational techniques Before this is done the idea should have the approval of physicians, for the public should and does look to physicians for judgment concerning a basic health concept of this kind If physicians will but test out the concept by teaching self-examination of the breasts to their own patients, I am confident that they will eventually give the idea their approval Some physicians will be tempted to condemn self-examination as a poor substitute for examination by a physician They should face the fact that there are few women who can go to a physician for physical examination often enough to hope to have breast carcinoma discovered at an early and curable stage To be reasonably safe a woman should be examined at least every two or three months Self-examination is the only possible method of achieving this It is a means of protection available to every woman, no matter how remote she may be from her physician It costs nothing

Physicians must also face the fact that the practice of self-examination will add to their difficulties in the differential diagnosis of lesions of the breast When women examine their own breasts they find a remarkable variety of tumors and tumor-like formations Most of these are the nodular thickening due to physiological changes in the breast and require no treatment, but some are small tumors due to disease that must be recognized as such and their pathological nature proved

The Role of the Physician in the Detection of Breast Disease

Physicians have an important opportunity to discover unsuspected disease in the breasts every time they examine the breasts in the course of a physical examination The value of careful routine examination of the breasts has been well proved in our clinic, where 4 9 per cent of the total number of breast carcinomas were found by such routine examination of patients who came to consult for some wholly irrelevant symptom We may take it for granted that when a physician sees a new patient and performs a physical examination, he will examine her breasts, but it is an unfortunate fact that this ideal is by no means achieved A survey conducted by the American Institute of Public Opinion in 1950 showed that when women went to physicians and asked specifically for a complete physical examination, in 30 per cent their breasts were not examined

A more excusable kind of failure to examine the breasts is that which occurs in the routine care of patients being treated for other disease As I have pointed out in Chapter 21, this kind of error might be avoided by making a rule to do a general physical examination upon old patients every six months

It is well also for physicians to remember that carcinoma of the breast develops

CHAPTER 5

METHODS OF DIAGNOSIS OF BREAST DISEASE

When breast disease has been detected either by the patient herself or by an examining physician the next step is to prove its nature In this task the physician depends upon three kinds of evidence—a proper medical history a careful physical examination of the breasts and when indicated a properly conducted biopsy Because the breasts are accessible organs situated on the surface of the body the symptomatology of disease in them can be to some degree defined, physical examination is relatively easy and biopsy is comparatively simple The requisites for the differential diagnosis of breast lesions are therefore generally available and inexpensive In the present chapter I will describe the methods I have come to rely upon

The Medical History

For convenience and completeness in recording the data in our cases in which breast carcinoma is suspected I devised the summary sheet shown at the end of this chapter It is used as a supplement to and not as a substitute for the regular clinical history in which the story of the patient s illness is recorded in her own words as brought out by understanding questioning The data recorded upon the summary sheet are arranged in such a manner that they can be transferred to punch cards and their correlations tabulated upon the International Business Machine The use of such a summary sheet makes certain that the pertinent clinical data, at least as we conceive of them today will be recorded

The first ten columns on the summary sheet are used for data which enables us to index and sort our cases according to unit record number year of admis sion hospital or Out Patient Department status, and primary or secondary classification

Columns 11 and 12 include nationality and national extraction Columns 14 and 15 deal with age and marital status Columns 16 to 19 record the data concerning pregnancy Columns 20 and 21 are devoted to the menstrual history Hormones are so widely used today that it is necessary to inquire regarding the patient s experience with them Column 22 serves this purpose The patient s lactation experience is recorded in Column 23 The family history as regards cancer in four generations is recorded in Column 24 Column 25 deals with the patient s nursing history Previous breast disease is recorded in Column 26

The check list of the important symptoms of breast disease as listed in Col umns 27 to 29 of the summary sheet is an important aid to the physician If he

concerning them is that they were found at a comparatively early stage, for the axillary nodes were involved in only 5, or 45 per cent, of the patients

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ing of the mechanism of hormonal control of lactation to know the exact nature of the physiological disturbances in these cases In several cases of continued and profuse lactation that we have studied both androgen and estrogen treatment were entirely ineffectual In most cases the continued secretion of milk is very slight in amount The few drops of milk that accumulate in the duct system may not escape spontaneously but appear only when the breast is squeezed or the nipple is stimulated This kind of discharge of milk is harmless and requires no treatment

A *serous discharge* is thin translucent and faintly yellowish It dries as a yellow stain upon the patient s brassiere or nightgown In the great majority of cases it is due to an intraductal papilloma growing in one of the larger ducts in the subareolar region Although the minute papillary processes of an intraductal papilloma are covered with epithelium serum escapes from them perhaps be cause they are easily traumatized. Infrequently a serous discharge occurs with carcinoma

The presence of a sufficient number of red blood cells to color a discharge brown or red necessitates classifying it as a *bloody discharge* This type of discharge is usually brownish in color Infrequently it resembles frank blood The bloody nature of the discharge has however no special significance like a serous discharge it is usually an indication of intraductal epithelial proliferation In the majority of cases this epithelial proliferation is benign It may be the papillary proliferation that is one of the components of cystic disease it may be the papillary proliferation accompanying duct dilatation resulting from abnormal or excessive stimulation by hormonal therapy but it is usually due to intraductal papilloma. In occasional patients with mammary duct ectasia a brownish or blood tinged nipple discharge occurs In rare instances there is slightly bloody discharge from the markedly engorged breasts of women in the last months of pregnancy Infrequently a bloody discharge is due to malignant intraductal epithelial proliferation as with intraductal papillary carcinoma

Another and less frequent type of nipple discharge is thin and watery without any color Lewison and Chambers present data suggesting that it signifies carcinoma.

A thick yellowish grayish or greenish nipple discharge suggesting pus sometimes occurs with low grade inflammatory processes situated in the subareolar region A drop of this kind of grayish or greenish discharge can not infrequently be expressed from breasts in which the central ducts are ectatic

In Columns 30 to 35 of my summary sheet I deal with the duration of symptoms, the delay in diagnosis and treatment and the responsibility for the delay It is important for us to attempt to be as exact as possible concerning this vital matter

The Physical Examination of the Breast

A good deal of the success which a physician has in the differential diagnosis of breast disease depends upon the care that he takes in the examination of the breasts If he merely passes his hand in a casual fashion over his patient s breasts as she sits erect, ready for an examination of heart and lungs he will often miss lesions of the breast entirely This kind of examination cannot give him any idea

runs down the list of symptoms after he has written his clinical history and circles the numerals opposite the symptoms noted by the patient he will make certain that none has been overlooked

An overwhelming proportion of patients discover their own disease, usually by finding a tumor The discovery is usually accidental, made while bathing or dressing Not infrequently trauma to the breast leads the patient to palpate it and she discovers a tumor which had been present before the trauma

Infrequently, patients discover their disease as a result of noting a change in the size, shape, or consistency of one breast, without appreciating the presence of a tumor as such Women are not, however, expert in detecting such changes and are usually not aware of them

Pain. Pain and tenderness, which are usually symptoms of physiological disturbance in the breast rather than of a neoplasm, are frequent complaints These subjective symptoms are not easy to evaluate Some comparatively unstable women, frightened of cancer of the breast, magnify minor physiological discomfort in the breasts to the point where they have to be periodically reassured or they are interminably miserable In a few women pain of physiological origin is in fact so severe that it is a major handicap

Occasionally, women who discover a tumor of the breast thereafter complain of a degree of pain in it Whether the pain is genuine and a natural phenomenon, or is the result of the repeated palpation to which patients often subject their tumors, or whether it is imagined, is sometimes difficult to judge In some women the first symptom is pain and tenderness, which are beyond all doubt genuine These symptoms are considerably more common in cystic disease than in any other type of breast tumor Both River and Corry have recently studied the frequency of pain in the various lesions of the breast My own impression is that pain and tenderness are so inconstant that they play little part in the differential diagnosis of diseases of the breast Their presence tends, if anything, to reassure the physician that his patient does not have carcinoma

Nipple Discharge. Discharge from the nipple is not a frequent symptom, occurring in only about 5 per cent of the patients with breast symptoms who consult me Nipple discharge may be physiological and harmless, or pathological and an indication of inflammation or epithelial proliferation Nipple discharge of pathological significance escapes spontaneously from the nipple Discharge that has to be elicited is not of pathological significance In many women of middle age squeezing the nipple and subareolar area will produce a drop of thick grayish material from the nipple If they discover this phenomenon they should be reassured and told that it is normal The examining physician has no need to attempt to express material from the nipple, and should not do so

The character of a nipple discharge is an important distinguishing feature There are two more common types of discharge—serous discharge, and bloody discharge Less frequently, nipple discharge may be thin and watery, or thick and yellowish, grayish or greenish resembling pus, or milky

A discharge that has the consistency and color of milk is usually just that. Occasional women continue to secrete a small amount of milk for months, and in rare cases for years, after lactation would normally have ceased A milky discharge of this kind is usually bilateral We do not yet have enough understand-

be felt When nodes are palpated in this region they are usually the more laterally and more superficially situated nodes that are involved by retrograde permeation from the sentinel nodes Supraclavicular palpation is therefore useful only for the detection of advanced regional lymph node involvement

In examining the axilla it is essential that the pectoral muscles be relaxed To achieve this the examiner supports the patient s arm on one of his own He palpates the axilla with the tips of the fingers of his other hand (Fig 67) The more gentle his palpation the better he will feel lymph nodes Small nodes high in the axilla are difficult or impossible to feel Nodes lying close behind the thick



Fig 67 Palpation of the axilla

body of the pectoralis major muscle as it forms the ventral wall of the axillary space are also easily missed In obese patients axillary palpation is particularly difficult.

Not only the number but the consistency and movability of the axillary nodes should be noted They may be fixed to the deep axillary structures or to the over lying skin It is also useful to estimate the transverse diameter in centimeters of the largest axillary node or mass of nodes

Even when the axilla is palpated with care and in the manner that I have sug gested palpation is notoriously inaccurate as a method of detecting metastasis In Table 8 which shows our Presbyterian Hospital data on this question it will

of the true character of the breast tissue An adequate examination of the breasts should be a studied and methodical procedure, requiring several changes in the patient's position, and meticulous palpation of the entire extent of the breasts, which cover most of the anterior chest wall This takes some time even when no abnormality is found When the examiner finds something that arouses his suspicion of the presence of disease still other maneuvers and more time are required



Fig 66 Palpation of the supraclavicular and cervical areas

Supraclavicular and Axillary Regions. The breast examination should be begun with palpation of the supraclavicular and axillary regions The patient sits on a table facing the examiner, with her legs over the side The supraclavicular and lower cervical areas are first carefully palpated (Fig 66)

It is important for the examiner to understand that metastasis in the so-called sentinel group of supraclavicular nodes, which lie upon the confluence of the internal jugular and subclavian veins hidden deep behind the inner end of the clavicle, are not palpable until they attain a large size In our supraclavicular biopsies we have often found metastases when no supraclavicular nodes could

Fig 68 Carcinoma metastasis in massively enlarged axillary lymph node

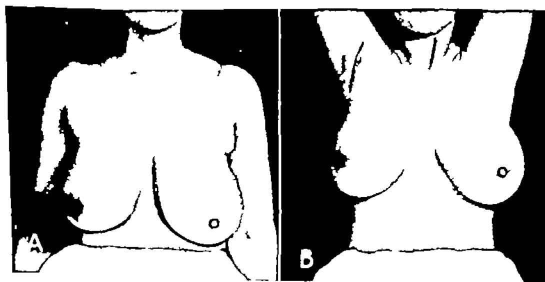


Fig 69 Inspection of the breasts. *A* with the arms at the side *B* with the arms raised.

Table 8 Frequency of Metastases in Axillary Nodes by Clinical Diagnosis
(Presbyterian Hospital 1915–1942)

Clinical diagnosis	Number of tumors	Number with axillary metastases	Per cent
Nodes not involved	578	269	46 5
Nodes involved	481	393	81 7
No diagnosis	58	28	48 3
Total	1117	690	61 8

be seen that in the patients with breast carcinoma in whom we thought there were no axillary metastases 46 5 per cent were, in fact, found to have them

In the patients in whom palpation led us to conclude that metastases were present, 81 7 per cent were found to have them on microscopical examination

Axillary lymph nodes that are massively enlarged, and by this I mean ones that measure 2 5 cm or more in transverse diameter, will almost always be found to contain metastases, as Table 9 shows In 105 patients with such massively enlarged axillary nodes there were only 2 in whom pathological study failed to show metastases. Figure 68 shows a massively enlarged metastatic node that measured 6 cm in diameter

Table 9 Frequency of Metastases in Axillary Nodes According to Their Size by Clinical Measurement
(Presbyterian Hospital 1915–1942)

Clinical measurement of lymph nodes	Number of operations	Microscopic slides available	Axillary metastases Number	Per cent
Nodes not palpable	422	416	177	42 5
Nodes moderately enlarged (less than 2 5 cm average diameter)	575	565	396	70 1
Nodes massively enlarged (2 5 cm or more average diameter)	106	105	103	98 1
Not described	32	31	14	45 2
Total	1135	1117	690	61 8

Inspection of the Breast The next step in our routine of breast examination is a critical inspection of the breasts, first with the patient's arms at her sides and then with her arms raised high above her head (Fig 69) The examination must be conducted in a good light if the examiner expects to see early retraction signs and slight changes in contour The examiner compares the contour of the two breasts, following it from the anterior axillary fold to the midline on each side An indentation or a bulge in the contour often betrays the site of the lesion

The shrunken breast of advanced, slowly growing carcinoma, and the generally enlarged edematous breast of acute carcinoma are at once obvious, but slight retraction signs due to earlier lesions are not so evident

Redness of the Skin Redness, and elevation of the skin temperature are of course seen with both acute and chronic infectious processes in the breast These signs also occur occasionally with neoplasms

The most striking example is the extensive redness of the skin in the so-called inflammatory type of carcinoma I will discuss this disease subsequently in Chapter 23

Redness of the skin of limited extent also occurs occasionally with the usual type of breast carcinoma, as the result of necrosis or infection within the lesion or due to impending ulceration



Fig 71 Edema of the skin of the breast due to tuberculosis of axillary lymph nodes.

With duct ectasia redness of the skin is to be expected when the irritating material within the ducts gets out into the breast stroma and sets up an inflammatory reaction

Redness of the skin is also seen in rare cases of cystic disease in which a subacute inflammatory reaction within the cysts develops Redness is therefore not pathognomonic of any special lesion in the breast.

Edema of the Skin Edema of the skin of the breast caused by blocking of the subdermal lymphatics develops in infections of the breast or axilla as well as in advanced carcinoma Lymph accumulates within the skin until it is several

It will occasionally be noted that one breast is slightly larger than the other, yet perfectly symmetrical with its mate This mere disparity in size is often only a developmental defect and no cause for alarm

The skin over the breast is carefully inspected, looking for dilatation of subcutaneous veins, redness, and edema

The shape and size of the areolas and their comparative level are noted The shape of the nipples and the axes in which they point are compared The surface of the nipples is inspected for crusting or erosion

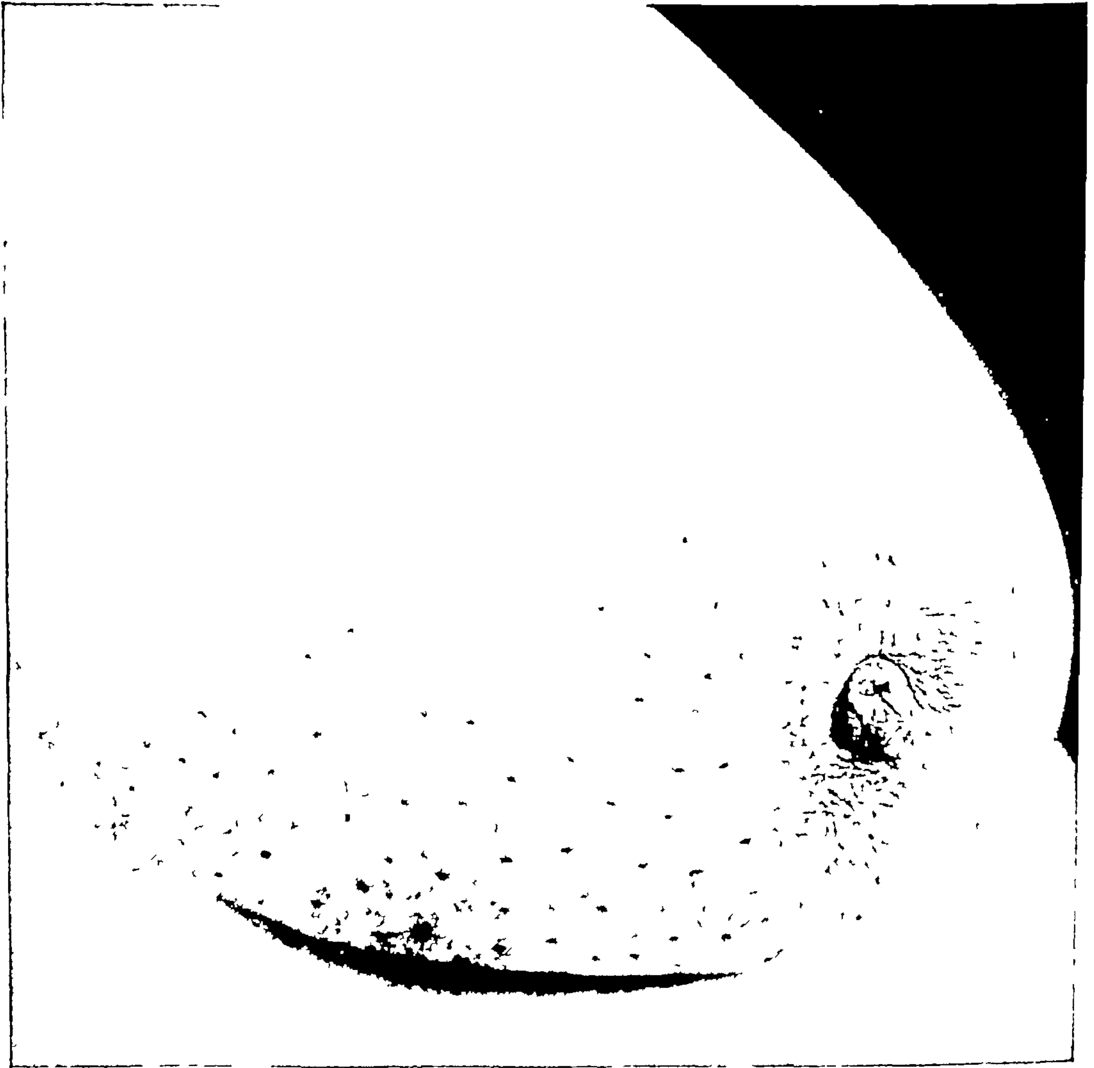


Fig 70 Extensive edema of the skin of the breast due to carcinoma

Dilated Subcutaneous Veins. Rapidly growing neoplasms in the breast, both benign and malignant, induce an increased blood supply to the organ Cystosarcomas seem to have a special tendency to cause enlargement of the regional veins In occasional patients with carcinoma the subcutaneous veins over the upper part of the breast may be visibly dilated Infrared photographs bring out this dilation in a striking manner

At operation the perforating branches of the internal mammary vessels at the intercostal level corresponding to the lesion will often be seen to be abnormally large

realize their significance and look carefully for them Occasionally benign eczematoid lesions of the areola are seen I will discuss the differential diagnosis of these lesions in Chapter 22, devoted to Paget s disease

It should at once be recognized, however that it is impossible to distinguish these non malignant erosions of the nipple and areola from Paget s disease on clinical grounds alone. All of them should be biopsied This may be done as an office procedure—excising a small wedge of the involved epithelium with local anesthesia

Palpation of the Breast

Inspection completed, the examiner is ready to palpate the breasts This is best performed with the patient lying down not sitting up For adequate palpa

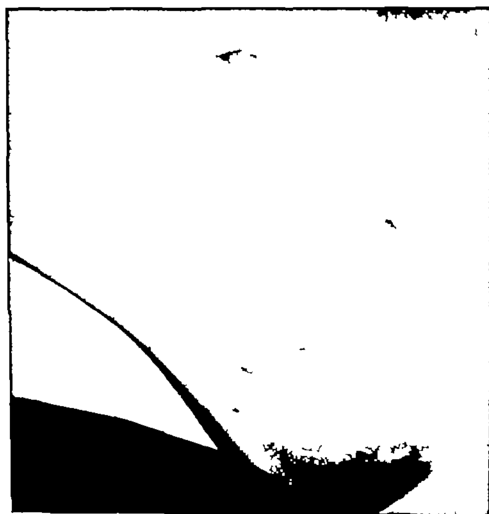


Fig 73 Ecchymosis of the skin of the lower outer sector of the breast following rough palpation

tion the breast should be balanced on the chest wall so that it forms as even a layer as possible flattened out upon the thoracic cage To achieve this we elevate the shoulder on the side being examined by placing a small pillow under it as for self-examination This throws the breast medially and tends to flatten it out upon the thorax. If the patient lies with her shoulders flat on the table, the breast

times its normal thickness and causes abnormal separation and deepening of the orifices of the cutaneous glands Figure 70 shows extensive edema of the skin over the breast due to carcinoma Figure 71 shows edema of the skin over the breast in a patient with tuberculosis of axillary lymph nodes

When the area of edema is small, as in the patient with carcinoma shown in Figure 72, it easily escapes detection unless carefully looked for It usually begins, as in this patient, in the skin within the areola, or just caudad to it, that is, in the most dependent part of the breast This is regularly the site where edema appears when the carcinoma is situated deep in the center of the breast, but it may also be the earliest location of edema when the carcinoma is situated in the



Fig 72 Edema limited to the skin of the areolar region in carcinoma of the breast

periphery of the breast We have seen edema appear just below and medial to the nipple when the carcinoma was a small one located in the upper outer part of the breast

There are, of course, other cases in which the edema first appears in the skin directly over a carcinoma situated more peripherally in the breast In such cases the skin is usually somewhat adherent to the underlying tumor, and it seems probable that the lymphatics of the skin are obstructed by direct retrograde invasion from the surface of the growth outward

Erosion of the Epithelium of the Nipple or Areola. Very small erosions of the epithelium of the nipple, measuring only a few millimeters in diameter, are often the only sign of the Paget's type of carcinoma These small erosions may not be seen and the opportunity for early diagnosis may be lost unless physicians

of the clavicle above, the midline of the sternum medially the lower edge of the inframammary fold caudad and the edge of the latissimus dorsi muscle laterally A small subcutaneous tumor near these outer limits of the breast may be mis taken for a benign subcutaneous *lesion not associated with the breast when* in

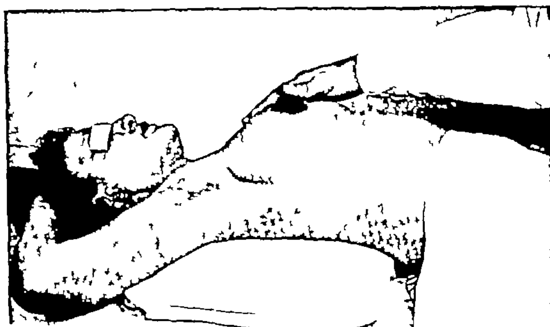


Fig 74 Palpation of the inner half of the breast arm raised above head.

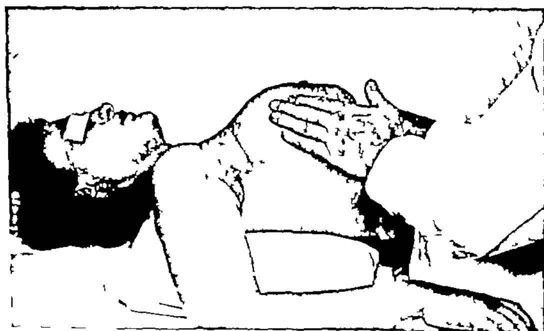


Fig 75 Palpation of the lateral half of the breast arm at side

fact, it is a carcinoma of the breast. The axillary prolongation of the breast extends high into the axilla in some women and a benign lesion or carcinoma arising in it is commonly mistaken for lymphosarcoma or adenitis of the axillary lymph nodes

Unless something is felt that arouses a suspicion of abnormality each area of

falls to the side and palpation of the lateral half is more difficult because this portion of the breast is folded upon itself and is correspondingly thicker

Palpation of the breast can and should be a gentle, precise, and orderly procedure Palpation must never be so heavy-handed that it distresses the patient Such an experience may deter her from returning for subsequent vitally important reexamination Gentle palpation is also more informative than rough examination Indeed, it can be said that the more gentle the palpation, the more informative it will be There is, moreover, a possible danger of causing metastasis by rough examination of a breast carcinoma I have seen patients whose breasts showed ecchymosis caused by rough examination Figure 73 shows such an area of ecchymosis in the lower outer sector of the breast which appeared following palpation by an enthusiastic surgeon A good many examiners have a deplorable tendency to paw at the breast in examining it, using both hands to knead it like a batch of bread in their anxious search for a tumor They are more likely to discover a tumor by precise and gentle palpation with the flat of the fingers of one hand

The whole extent of the breast, as it lies relatively flattened out and balanced upon the chest wall, should be palpated systematically with the flat of the fingers of one hand It is convenient to begin with the medial half of the breast In palpating this area of the breast, it is advantageous to have the arm raised above the head (Fig 74), a position that tenses the pectoral muscles so that it provides a flatter surface upon which the breast rests The examiner's fingers trace a series of parallel transverse lines across the medial half of the breast from the nipple line to the sternum, beginning at the clavicle and ending at the inframammary fold

Palpation of the lateral half of the breast is best carried out with the patient's arm at her side (Fig 75) In this position the breast lies more caudad and its lateral half is more accessible to palpation The examiner's fingers again trace a series of parallel transverse lines across this half of the breast from the posterior axillary line to the nipple line, beginning at the inframammary fold and ending in the infraclavicular region

One of the features of the normal anatomy of the breast which may confuse the examiner is the *inframammary fold* In the more turgid breasts of adolescents and younger women who have not borne children no inframammary fold is found But in the more flabby breasts of older women, and particularly in larger breasts, a prominent inframammary fold is often palpable It forms a transverse ridge of denser nodular tissue at the caudad edge of the breast Here the mammary tissue is bound down tightly to the deep fascia of the thoracic wall, compressed between the superficial and deep layers of the superficial fascia The weight of the dependent bulky breast folds down over and presses upon it, and produces in it a degree of congestion or fibrosis sufficient to make the lower edge of breast tissue palpable as a ridge This ridge may be so prominent in some patients that it is mistaken for a tumor due to disease It is not infrequently slightly tender A tightly fitting brassiere may be a factor in accentuating the inframammary ridge

In examination of the breasts it should be kept in mind that the breast tissue often extends over a very wide area A thin sheet of it may reach the lower edge

is not infrequently mistaken for a tumor in such breasts On the other hand, a real tumor of small size situated in the subareolar tissue or just caudad to the areola in such a thick dense breast may be almost impalpable in the supine position while it is readily felt when the breast is examined between the fingers with the patient in the sitting position

In some patients the presence of a single sharply defined dominant tumor in an otherwise unremarkable breast leaves no doubt in the examiner s mind as to the presence of disease But in many other patients the findings of palpation are not as conclusive and the examiner has difficulty in interpreting what his fingers feel in the breast In these patients he has to attempt to answer the question—*is the nodularity which he feels within the limits of the normal physiological variation in breast structure* or does it represent a *dominant tumor due to inflammatory or neoplastic disease?* If it is the former no intervention is of course indicated while if it is the latter surgical investigation is imperative

In keeping with its lobular structure the normal breast has a finely nodular character on palpation With increased engorgement and with perhaps other physiological changes which we do not understand the coarseness of the nodules may be considerably increased. When such breast tissue is studied histologically nothing abnormal is seen and the conclusion is inescapable that the increased nodularity is a physiological and not a pathological change Such increased nodularity may be generalized throughout the breast but it is often more or less limited to one sector The nodularity may be so marked that it becomes very difficult to decide whether or not it constitutes a dominant tumor representing disease

In general it may be said that disease usually takes the form of a single dominant tumor while the increased nodularity due to physiological change involves a considerable area in one breast or several sectors in both breasts An exception must be made of course for cystic disease which often produces multiple tumors A localized area of increased nodularity representing nothing more than physiological change may give the impression of a dominant lump The differentiation of this kind of an area from a tumor representing real disease is the most difficult decision that an examiner has to make It must be said that many surgeons tend to take refuge in the easy philosophy of operating when in doubt because this safeguards the patient The result is that a large number of needless operations are performed upon the breast. The only hope that surgeons will improve their diagnostic accuracy lies in teaching them to examine the breasts with greater care and correlate their impressions from physical examination with the findings of their pathologists I shall deal in detail with this matter of correlation of physical and pathological findings in my chapter on cystic disease

The examiner needs not only a method for palpation such as I have outlined but a system for expressing and for recording his tactile impressions of the lesion in terms of five physical qualities that tumors exhibit namely *size shape delimitation consistence* and *movability within the breast tissue*

The *size* of the tumor should be determined and recorded in centimeters by finding the tumor edges with two *fingers and measuring* the distance between them with a rule or tape If the tumor is round one diameter will suffice but if it is discoid or elongated two or more diameters should be recorded The clinical

the breast need be palpated but once The examiner should aim at minimizing his palpation, gentle though it may be When the patient is referred to a surgeon, he must palpate both breasts once more to provide a complete case record, but repeated palpation by other physicians and by students should not be permitted

When palpation of the breast is carried out in warm weather and the skin is moist, a little talcum powder on it diminishes friction and adds to the accuracy of tactile perception

I have learned that palpation with the patient erect is an inaccurate method of examining the entire breast The upper outer sector of the breast, where neoplasms are most frequent, is not conveniently accessible in this position



Fig 76 Incorrect method for palpation of the breast

Unless the breast is small it hangs down and folds upon itself when the patient is erect, and in this dependent position it is thicker and more difficult to palpate than when it is flattened out upon the chest wall of the supine patient Figure 76 shows how *not* to examine the breast

The subareolar region and the portion of the breast just caudad to the areola, however, are areas which, in patients whose breasts are large, should be palpated with the patient sitting erect, as well as in the supine position In the subareolar area, where the ducts converge to enter the base of the nipple, the breast structure is normally comparatively looser and less dense In breasts that are thick and relatively firm in texture, the comparatively denser breast tissue of the upper half of the breast forms a sort of ledge above the softer subareolar region This ledge

is not infrequently mistaken for a tumor in such breasts On the other hand, a real tumor of small size situated in the subareolar tissue or just caudad to the areola in such a thick dense breast may be almost impalpable in the supine position while it is readily felt when the breast is examined between the fingers with the patient in the sitting position

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measurements made in this way will be found to be about 1 cm greater than the pathologist's measurements of the tumor in the operative specimen, due to the added thickness of the surrounding breast tissue I can only deplore tumor size expressed in terms of fruits, nuts, or vegetables, but I have to admit that even present day medical students, who presumably have had a scientific education, continue to prefer these agricultural terms to the metric system

The *shape* of tumors, whether rounded, discoid, elongated, nodular, or irregular, should be recorded Most tumors when very small tend to be rounded, but when they become larger they often have more or less characteristic shapes For example, cysts are usually round, adenofibromas may be rounded or discoid, while carcinoma is often irregular in contour

A very important quality is *delimitation* By delimitation I mean the degree of sharpness with which the edges of the tumor are felt This quality might be called demarcation, or circumscription, but delimitation is perhaps a more exact term Cysts and adenofibromas are usually well delimited in the breast tissue The edges of an area of adenosis, fibrous disease, or carcinoma, on the other hand, are not felt as sharply They seem to fade out into the surrounding breast tissue This lack of delimitation is due to the infiltrative character of these lesions

There are, however, exceptions to these generalizations An area of increased nodularity due to physiological change, or a tumor formed by a multitude of minute cysts may be poorly delimited In contrast, there are several types of carcinoma that are often remarkably well delimited—the type that we classify as the circumscribed form, papillary carcinoma, and well differentiated intraductal carcinoma

The *consistency* of lesions in the breast is not always a reliable guide but it is certainly one of the most helpful indications of their nature Most cysts have an elastic quality, some of the larger ones can be felt to fluctuate, and others are so soft that they can be felt only with the gentlest palpation Very tense cysts may, however, be quite firm Most carcinomas have a wooden hardness, but a calcified adenofibroma is equally hard Papillary carcinoma may be soft Adenosis may be almost as firm as carcinoma An area of increased nodularity due to physiological change is usually not as firm as carcinoma It is impossible to estimate accurately the consistence of very small tumors

The degree of *movability* of a tumor in the breast tissue which surrounds it is perhaps the best guide to its nature Fibroadenomas and cysts have the greatest degree of movability Indeed, they often seem to be so freely movable, and slip about so readily under the fingers of the examiner, that he is at once convinced of their benignancy Carcinoma, adenosis, and fibrous disease, on the other hand, are relatively fixed in the breast tissue in which they lie They cannot be much moved about, as would be expected from their infiltrative nature An area of increased nodularity due to physiological change is often intermediate in its movability It is not as freely movable as a cyst or adenofibroma but it is by no means as fixed as a carcinoma

It is important for the examiner to be objective about his findings in palpation of the breast In order to discipline myself in objectivity I make it a rule when I begin to take my patient's history to ask her *not* to tell me in which breast, and in what part of the breast, the tumor is situated When I have finished my palpa-

tion if I have found a tumor I ask her if it is the one she or her previous examiner had found If I have found no tumor I tell her so and ask her to show me any tumor she or a previous examiner may have felt It has been a humiliating experience for me on a number of occasions to have the patient demonstrate a definite tumor after I had missed it. This experience may humiliate the examiner but it may save the patient s life if the tumor is a carcinoma It is I am sure a sound rule for the physician to check his findings with the patient s As I have

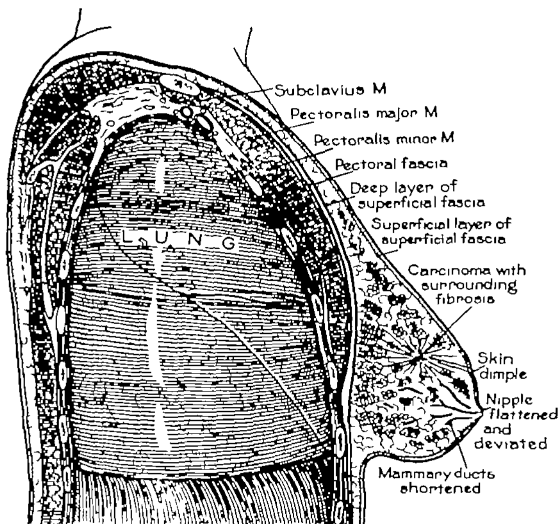


Fig 77 Diagram of parasagittal section through the breast to illustrate the mechanims of retraction.

already pointed out women can be very accurate indeed in palpating disease in their own breasts

Another important safeguard in the diagnosis of breast lesions is to question the validity of conclusions based on palpation if the patient is examined during the premenstrual or menstrual phase of her cycle Engorgement is so marked in some patients during these phases of the cycle that innocuous increased nodularity may give the impression of a dominant tumor due to disease When there is any question as to the nature of the breast lesion in a patient examined during these unfavorable phases of her cycle, she should be asked to return for a reexamination as soon as menstruation is over Cysts not infrequently enlarge with

striking rapidity in the premenstrual phase of the cycle and decrease sharply in size after menstruation When an observing patient reports this phenomenon it is strong evidence in favor of cystic disease

Palpation provides the most important evidence in the diagnosis of breast lesions, but a search for retraction signs is also an essential part of an adequate examination of the breast in patients in whom there is any indication of breast disease It is the next step in the examination of the breasts



Fig 78 Marked retraction produced by carcinoma of upper central portion of breast

Retraction Phenomena in the Breast

Retraction signs constitute a whole series of clinical manifestations ranging from a small dimple in the skin over the tumor to shrinkage of the entire breast They are due to the fact that the growth of neoplasms, or the evolution of inflammation from bacterial infection or fat necrosis, causes proliferation of fibroblasts not only within the lesion itself but into the surrounding breast tissue This scar tissue, so to speak, contracts as it grows older, and since the breast is normally loose and fatty in structure, any or all of the tissue adjacent to the lesion may be pulled in toward it by the shortening strands of fibroblasts This phenomenon is of fundamental importance in the interpretation of the clinical signs that disease produces

This mechanism, by which carcinoma produces retraction phenomena, is illustrated by the accompanying drawing of a parasagittal section through the chest and the breast in the nipple plane (Fig 77) I have already pointed out that the breast lies very close to the skin between the superficial and deep layers of the superficial fascia The fascial septa of the breast, the so-called Cooper's ligaments, are intimately connected with this enveloping fascia Superficially this fascia is attached to the skin and deeply to the pectoral fascia The fibrosis within the carcinoma and radiating out around it exerts an abnormal traction upon these fascial septa of the breast. They pull the skin inward to produce



Fig. 79 Broad shallow dimple in skin over carcinoma of upper outer sector of breast.

dimpling and they fix the breast to a varying degree to the underlying pectoral fascia, limiting its movability and distorting its contour If the pectoral muscles are contracted carrying the pectoral fascia cephalad the sector of the breast in which the carcinoma lies is pulled upward abnormally and its contour distorted Contraction of the pectoral muscles may likewise bring out dimpling of the skin over the carcinoma because of the abnormal fixation of the pectoral fascia to the carcinoma, and of the carcinoma to the overlying skin by the fibrosis around it When the fibrosis involves the larger mammary ducts, they are shortened with the result that the axis in which the nipple points is changed or the nipple is flattened and finally retracted.

A good example of pronounced retraction is illustrated in Figure 78 Here,

the carcinoma is situated in the upper central portion of the breast just above the areola The skin over it has been drawn inward, forming a deep dimple The areola has been pulled upward toward the carcinoma and, in its upper part, it is so narrowed that it is hardly discernible The nipple is also pulled upward, and its axis deviated so that instead of pointing forward and somewhat laterally, it points upward toward the carcinoma

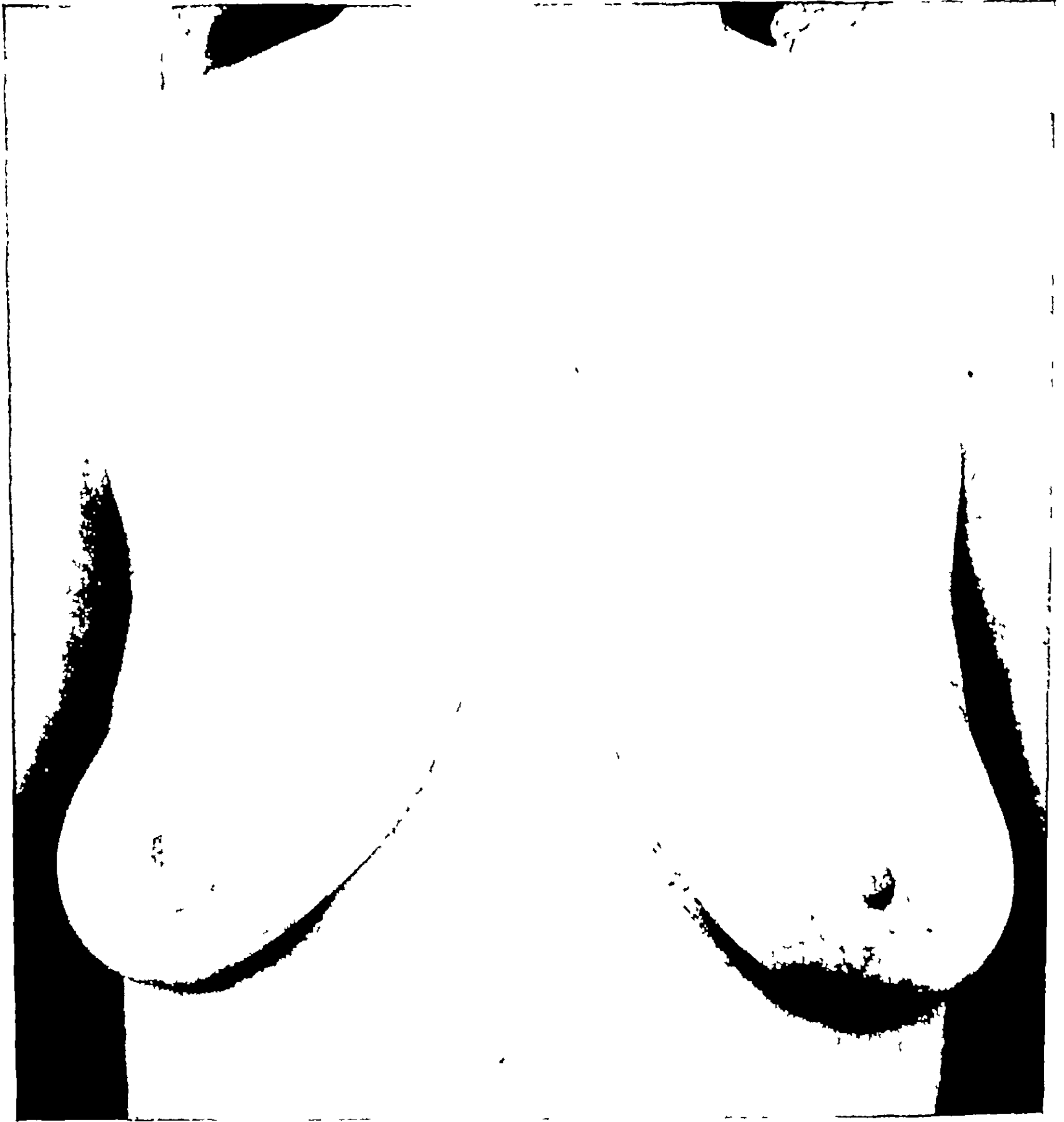


Fig 80 Breasts symmetrical with arms at sides, in carcinoma of the inner lower sector of the right breast

Another example of a dimple in the skin over a carcinoma of the breast is shown in Figure 79 Here the dimple is a broad, shallow one Again, the areola and the nipple are pulled upward toward the carcinoma

These retraction signs are often less well developed They may be so subtle that they can only be demonstrated by certain maneuvers

The simple act of *raising the arms high above the head* will sometimes reveal asymmetry of the breasts, or retraction of the skin, which is of decisive diagnostic significance Figure 80 shows a 30 year old patient in whom no asymmetry of

the breasts is evident as she sits with her arms at her sides In Figure 81 which shows her with her arms raised a well-defined indentation is seen in the inner lower sector of the right breast adjacent to the small tumor indicated by the circle. As this fact suggests, the tumor was a carcinoma The fibrosis around the carcinoma has attached it abnormally closely to the underlying pectoral fascia and to the overlying skin When the arms are raised, elevating the pectoral fascia,

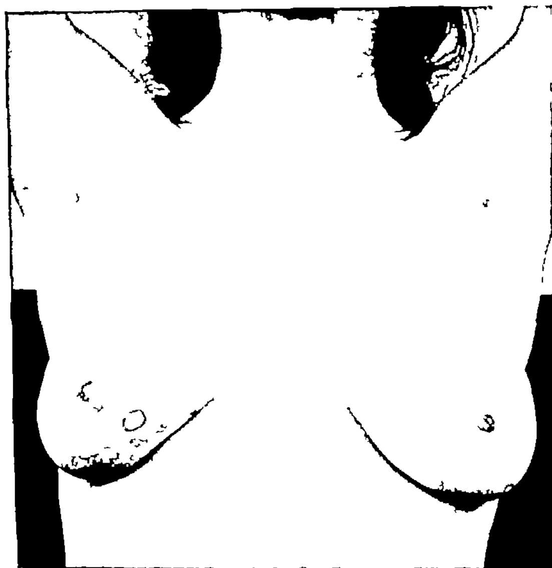


Fig 81 Indentation in the contour of the breast, with arms raised, in carcinoma of the lower inner sector of the right breast indicated by the circle marked on the skin

the carcinoma and the overlying skin are pulled upward and inward to a greater degree than the surrounding normal breast, producing the telltale asymmetry

Another maneuver that is useful in revealing retraction of the skin is for the examiner to *lift the breast upward* with his hand When the lesion is in the upper half of the breast this maneuver will often bring out a dimple in the skin over it although none is seen when the breast hangs dependent. The mechanism of this phenomenon is a simple one The skin over the lesion is tied down to it by fibrosis, while the skin over the normal surrounding breast lifts freely

A variant of this same maneuver is *molding the breast* around the tumor The

examiner's fingers gently lift the breast up around the tumor, as shown in Figure 82 Here the carcinoma was situated in the upper outer sector of the breast The dimple over it thus demonstrated is plainly seen Dimpling occurs because the skin is tied down to the carcinoma by fibrosis, while the surrounding skin and breast tissue is elevated by the pressure of the examiner's fingers Jackson and Severance have recently called this maneuver the "plateau test " When the tumor is in the lower half of the breast, this same maneuver, carried out with the patient lying down, will often bring out a dimple over the lesion, as shown in Figure 83



Fig 82 Dimple over carcinoma in the upper outer sector of the breast demonstrated by gentle molding of the breast tissue around the tumor

Another maneuver that is often helpful in demonstrating retraction signs is that of *pectoral contraction* While in the sitting position, the patient relaxes and rests her hands on her hips, giving the examiner an opportunity to compare the relative height of the lower edge of the breast and the level of the areola on each side, and to look for retraction signs over the tumor The patient is then asked to press her hands against her hips, contracting her pectoral muscles, first on the normal and then on the diseased side The normal breast is pulled upward slightly by this motion, but the carcinomatous breast often rises sharply as compared with its mate The breast as a whole may be abnormally elevated, or merely the sector of the breast in which the carcinoma is situated This abnormal elevation occurs, of course, because the fibrosis in the carcinomatous area fixes it abnormally to the underlying pectoral fascia When contraction of the pecto-

ralis major elevates the pectoral fascia, the carcinomatous area in the breast is pulled up with it.

Pectoral contraction also brings out other retraction signs—deviation of the nipple toward the tumor and furrows and dimples in the skin over it Figures 84 and 85 demonstrate this pectoral contraction maneuver in a patient with a carcinoma in the outer upper part of the breast Figure 84 shows the patient with her hand resting relaxed on her hip no definite dimpling is seen in the skin ad



Fig. 83 Dimple in lower half of the breast, demonstrated by gentle molding of the breast tissue around the tumor

jacent to the carcinoma indicated by the circle But in Figure 85 when her hand is pressed against her side contracting the pectoral muscle a whole series of furrows appear in the skin

This is of course a rather marked example of skin dimpling brought out by pectoral contraction Careful scrutiny should detect less well-developed dimpling, as in the patient shown in Figures 86 and 87 In Figure 86 where the hand is not pressed against the hip no dimpling is seen over the carcinoma which is situated in the outer middle sector of the breast In Figure 87 in which the pectoral muscles are contracted two small dimples are seen over the tumor

Another procedure of great value in demonstrating retraction signs in the breast is the *forward-bending maneuver* I learned of it from the late Hugh Auchincloss The patient is asked to stand and bend far forward from the hips, keeping her chin up and extending her hands toward the examiner who supports them on the tips of his own fingers as he sits before her (Fig 88) In this position, normal breasts fall freely away from the chest wall and are perfectly symmetrical But if a lesion producing retraction is present in one of them, even though it be



Fig 84 Pectoral contraction maneuver—arm resting on hip Carcinoma of the upper outer sector of the breast

small, the fibrosis that accompanies it will usually fix the diseased breast to the chest wall in some degree and produce an asymmetry that careful inspection from the side or from the front will detect Over and over again, we have seen carcinoma in the breast betrayed by asymmetry demonstrated in this maneuver, although there were no other retraction signs Figures 89 and 90 show a good example of the value of forward bending There was a small carcinoma beneath the right areola, but no asymmetry was evident as the patient stood with her arms at her sides When she bent forward, however, the nipple and medial part

of the right areola were pulled up deeply into the breast No examiner could miss the distortion

Figures 91 and 92 show another patient in the erect and forward bending positions and illustrate how forward bending accentuates the retraction signs produced by a carcinoma in the upper middle sector of the breast. Note how the right breast is held up against the chest wall and its areola and nipple deviated laterally in the forward bending position

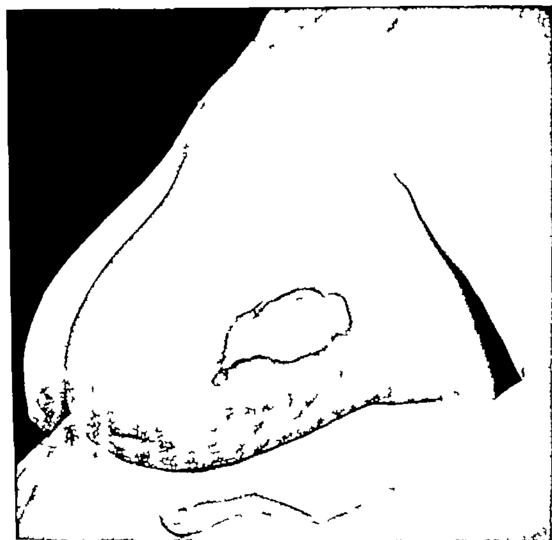


Fig 85 Pectoral contraction maneuver—arm pressed against the hip bringing out furrows in the skin over the carcinoma.

The change that carcinoma produces in the contour of the breast in the forward bending position is sometimes less obvious in patients with more dense less atrophic breasts In such breasts forward bending may reveal only a slight flattening of the contour of the breast adjacent to the carcinoma

Fixation of the Breast

As carcinoma of the breast extends locally the tumor itself as well as the breast in which it lies tends to become fixed to the underlying pectoral fascia and muscle and finally to the thoracic cage It is important to define this fixation

in terms of degree All surgeons are familiar with the advanced degree of fixation in which the breast is immovable upon the chest wall But the early stages of the process often escape the examiner's attention, for they are brought out only by certain special maneuvers

It has been my custom to classify fixation in three degrees The first two degrees are somewhat different manifestations of abnormal attachment of the carcinoma



Fig 86 Pectoral contraction maneuver—arm resting on hip *Carcinoma of the middle outer sector of breast*

to the underlying pectoral fascia and muscle Third degree fixation is evidence of attachment of the tumor to the tissues of the chest wall beneath the pectoral muscle, or to the tissues of the chest wall *lateral to the pectoral muscle*

First degree fixation is demonstrated with the patient sitting erect She places her hands against her hips and contracts her pectoral muscles by pressing her hands against her hips The breasts, if they are not too heavy, are normally pulled upward slightly by this action But when carcinoma has produced abnormal

fixation of the breast to the underlying pectoral fascia or muscle, the diseased breast is pulled upward to an abnormal degree, or in an asymmetrical manner Figure 93*A* shows a marked example of first degree fixation Pectoral contraction caused a 2 cm elevation of the tumor and accentuated the skin dimpling Such abnormal elevation may be apparent only along the lateral aspect of the breast



Fig 87 Pectoral contraction maneuver—arm pressed against the hip bringing out small dimples in the skin over the carcinoma

if the tumor is situated in its outer half In these patients with only first degree fixation the breast, the tumor within it can still be moved passively with freedom over the chest wall when the patient lies supine with the pectoral muscles contracted

Second degree fixation is demonstrated with the patient lying supine with her hands placed upon her hips With the pectoral muscles relaxed the examiner gently tests the passive mobility of the tumor over the chest wall, as shown in

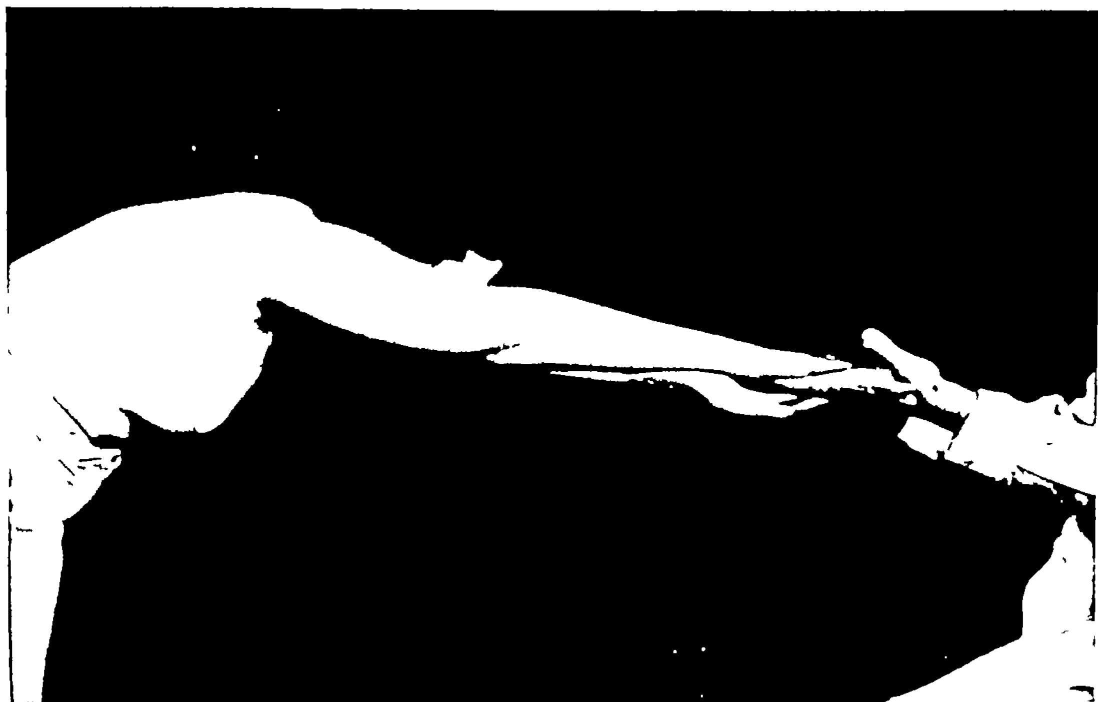


Fig 88 The forward bending maneuver

Fig 89 Breasts symmetrical in erect position—carcinoma of the right subareolar region.

Fig 90 Retraction of areola and nipple in forward bending position. Carcinoma of the right subareolar region.

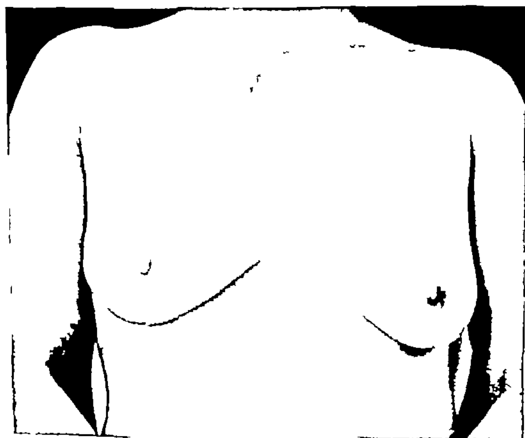


Fig 91 Right breast slightly elevated but otherwise symmetrical in erect position—carcinoma of the upper central region of the right breast

Figure 93B The patient is then asked to press her hands against her hips to contract the pectoral muscles In those patients with what I call second degree fixation, the movability of the tumor between the examiner's hands upon the chest wall will be sharply checked as the pectoral muscles are contracted It is my impression that abnormal fixation of the tumor to the pectorals, as demonstrated by this maneuver, represents a more advanced stage of fixation than the phenomenon that I have described as first degree fixation

Third degree fixation in my classification is the advanced stage when carcinoma is immovably fixed to the chest wall, even when the pectoral muscles are relaxed



Fig 92 Right breast held up against chest wall, its areola and nipple deviated laterally, in forward bending position—carcinoma of the upper central region of the right breast

Retraction Signs in Nipple and Areola

In his search for retraction signs, the examiner should pay special attention to changes in the areola and nipple The horizontal levels of the areola and nipple are often elevated by a carcinoma in the upper half of the breast

Deviation of the axis in which the nipple points is a subtle retraction sign The fibrosis in and about the lesion pulls on the duct system and tilts the nipple so that it points toward the tumor Figure 94 shows deviation of the axis of the right nipple upward and laterally toward a carcinoma of the upper outer sector of the breast

When the lesion involves the area more or less directly beneath the nipple, the

fibrosis shortens the whole duct system and pulls the nipple inward In carcinoma this process may show itself merely as flattening and broadening of the nipple (Fig 95) on the carcinomatous side as compared with its mate As the fibrosis progresses, the nipple becomes flatter and broader until in some instances, it is finally retracted beneath the surface of the surrounding areola (Fig 96) Nipple retraction is also seen in benign lesions producing fibrosis in and about the collecting ducts particularly in *ectasia of the ducts*

The fibrosis following an abscess sometimes distorts the nipple, changing its



Fig. 93A. A marked example of first degree fixation of tumor to pectoral fascia. Carcinoma of upper inner sector of breast. Contraction of pectoral muscle elevated the tumor 2 cm. and accentuated the skin retraction.

axis or retracting it The history and the presence of a scar should enable the examiner to interpret such changes correctly

Flattening or retraction of the nipple caused by these lesions should not be confused with mere *inversion of the nipple* a condition seen in a good many women with no disease of the breast. Inversion of the nipple may be bilateral or unilateral The patient will usually say that the inversion has been present for many years and that it interfered with nursing Instead of protruding in the normal way the nipple is hidden in a sulcus from which it can usually be pulled out. Figure 97 shows an inverted nipple in a woman aged 67 that had been inverted since she was 30 years of age There was no disease in her breast. The inverted nipple is not broadened and thickened and fixed as is the nipple retracted by disease

Fig 93B Testing mobility of carcinoma of the breast to determine second degree fixation

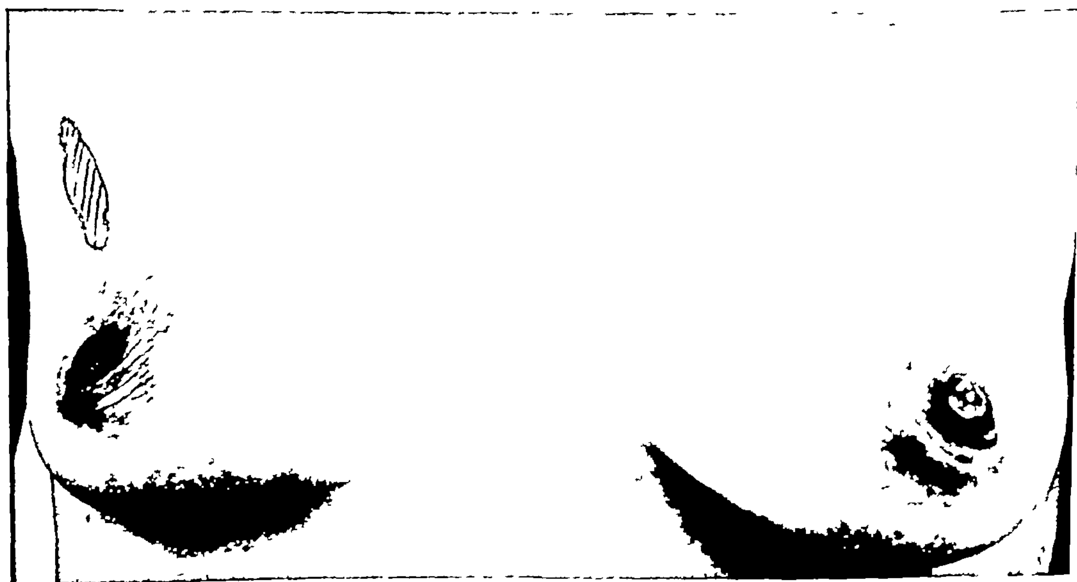


Fig 94 Upward and lateral deviation of right nipple—carcinoma of the upper outer sector of the right breast

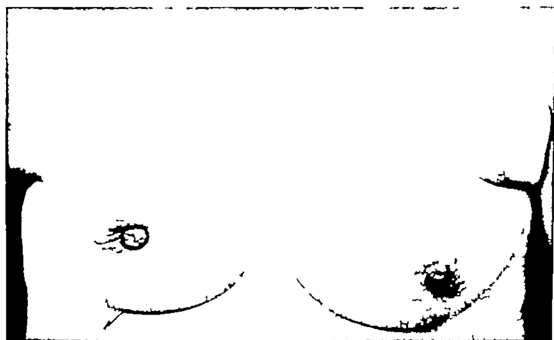


Fig. 95 Flattening and broadening of the nipple produced by carcinoma of the central region of the right breast.



Fig 96 Retraction of nipple below the surface of the areola in carcinoma of the centra portion of the breast.

Carcinomas of the breast in which a careful examination fails to reveal any of the retraction signs described are few indeed In my experience these few have been either the papillary the circumscribed or the well-differentiated type These varieties seem to produce less fibrosis in the surrounding breast than most carcinomas and therefore, less retraction

Although I have described retraction signs in general as being due to carcinoma it should never be forgotten that benign lesions also produce retraction Duct

ectasia, in particular, may produce very marked retraction signs that can deceive the most experienced clinician into thinking that he is dealing with carcinoma. Any of the benign lesions of the breast may on occasion produce retraction of the skin Benign lesions of the breast which form a considerable mass, and sometimes protrude slightly above the level of the adjacent breast, not infrequently produce a sort of pseudoretraction of the adjacent skin This effect is merely the result of the contrast between the skin over the protruding tumor and the skin

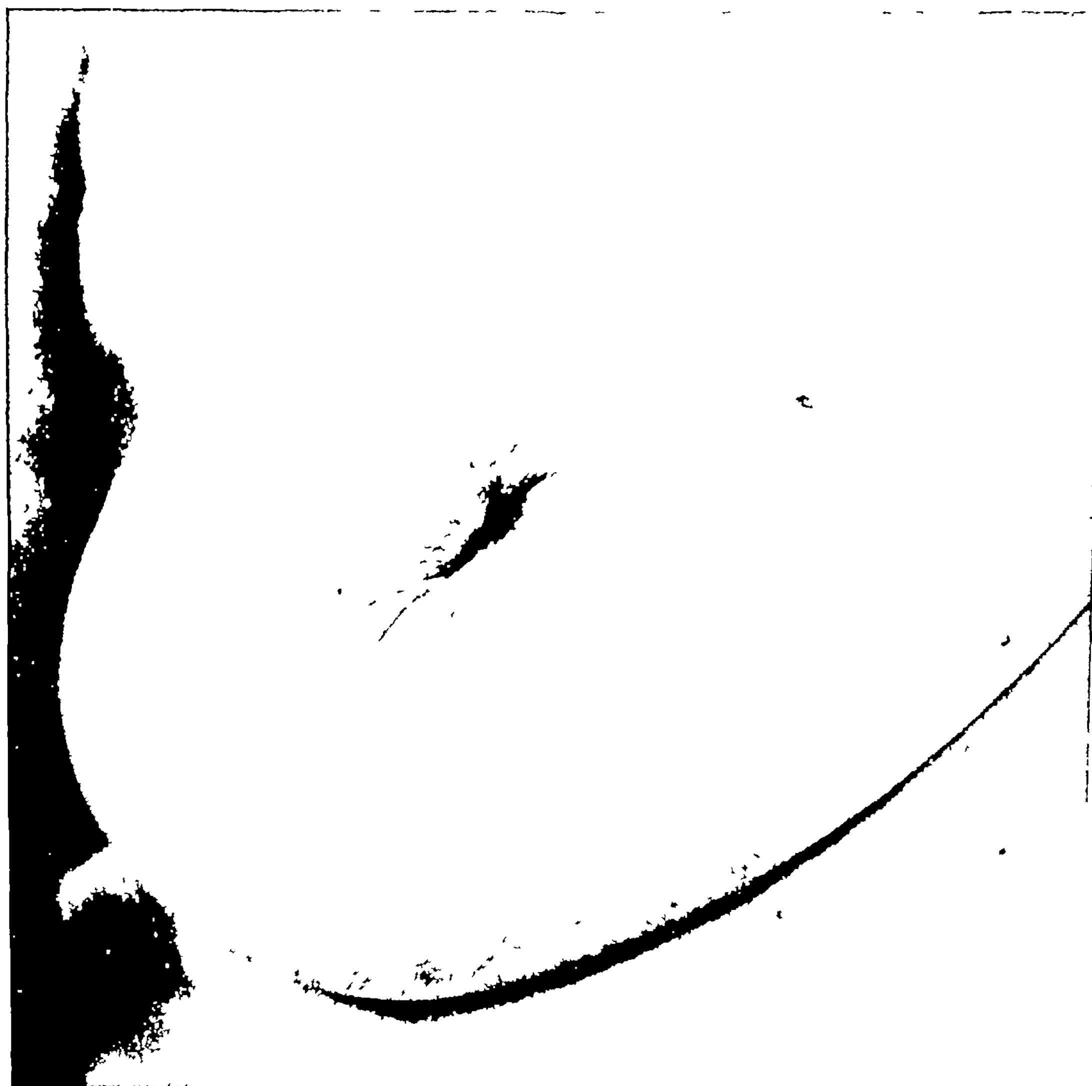


Fig 97 Simple inversion of the nipple—no disease of the breast

over the adjacent breast Figure 98 shows such pseudoretraction just caudad to a large benign intraductal papilloma

On the summary sheet for breast carcinoma which we employ, Columns 36 to 46 are used to record the findings of physical examination in a manner suitable for studying correlations from punch cards Checking these items off one by one on the summary sheet helps the clinician make certain that he has not forgotten anything important

In addition to filling out the summary sheet it has been my custom to make a sketch of the breast in each patient, and to indicate on it my physical findings These sketches are very simple and have no pretension of artistic merit The

effort to draw what I see however makes me look more sharply for retraction signs and it helps to fix in my mind the site and characteristics of the lesion I draw the outline of the breast in black ink and put the lesion in in red ink If the tumor is well delimited it is drawn with a solid line Poorly delimited lesions are indicated by crosshatching if they form a uniform mass while they are indicated by a cluster of coarse dots if they are nodular Foci of coalescent nodules are shown by short curved lines within the dotted area as in Figure 99 Figure 100 reproduces my sketch of a round sharply delimited tumor that proved to be a cyst.

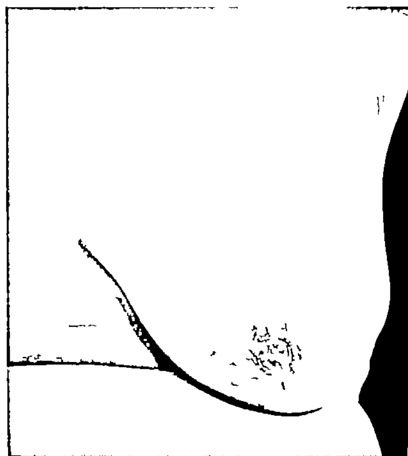


Fig. 98 Pseudo-retraction of the skin caudad to a benign intraductal papilloma of the breast.

Figure 101 shows my sketch of a poorly circumscribed tumor indicated by crosshatching that proved to be a carcinoma. Retraction, as evidenced by linear depressions in the skin deviation of the nipple toward the tumor and distortion of the areola were sketched in as seen

I make a notation on the sketch as to the size of the tumor in centimeters its shape its delimitation its consistence, its movability and whether or no retraction signs are seen

The Site of the Tumor within the Breast

Recent evidence, which I will present in Chapters 19 and 26 indicates that carcinomas situated in certain portions of the breast are more likely to metastasize to the internal mammary lymphatic chain as well as to the liver and prob-

ectasia, in particular, may produce very marked retraction signs that can deceive the most experienced clinician into thinking that he is dealing with carcinoma. Any of the benign lesions of the breast may on occasion produce retraction of the skin Benign lesions of the breast which form a considerable mass, and sometimes protrude slightly above the level of the adjacent breast, not infrequently produce a sort of pseudoretraction of the adjacent skin This effect is merely the result of the contrast between the skin over the protruding tumor and the skin

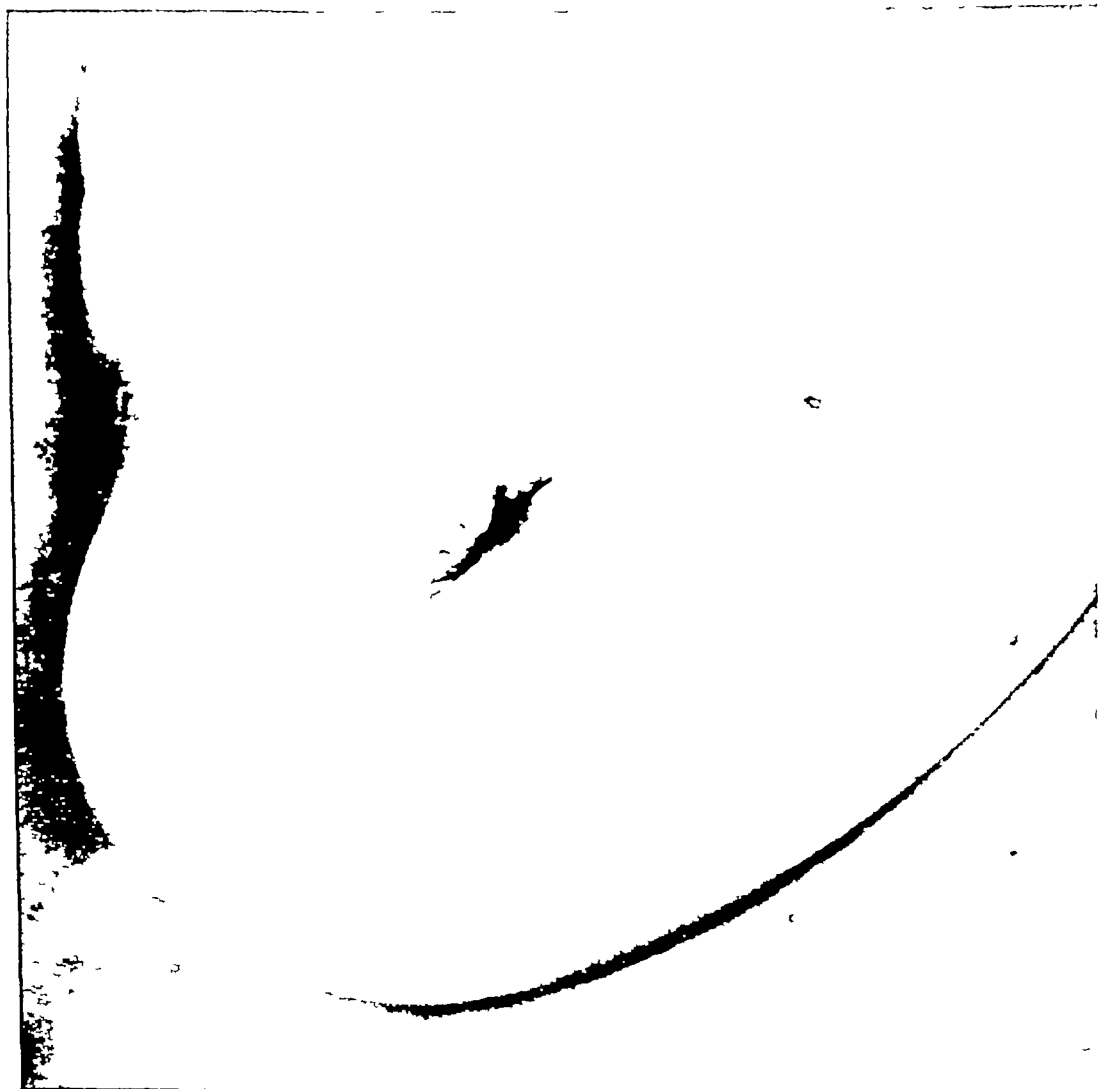


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For the purpose of classifying breast carcinomas according to sites which appear to have some special significance in terms of their natural history we have divided the breast into 7 zones A B C D E, F and G, as indicated in Figures 102 and 103 Any tumor lying beneath the areola or any tumor whose edge reaches within 1 cm of the edge of the areola is classified as a central or zone G tumor and is presumed to be in contact with the rich subareolar lymphatic plexus The upper and lower *parasternal* zones zones D and E, are defined as zones limited medially by the midline of the sternum and laterally by a vertical

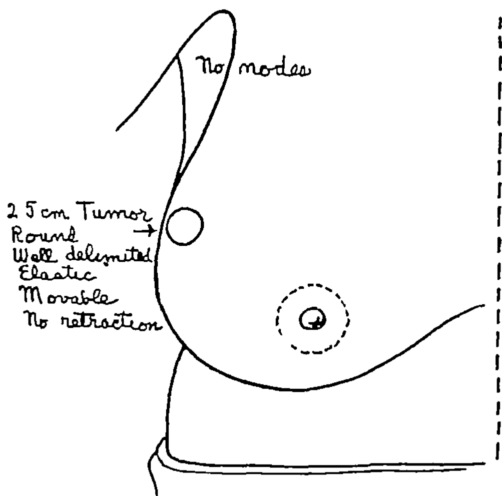


Fig 100 Sketch of the physical findings in a cyst of the breast.

line drawn 3 cm lateral to the sternal edge The horizontal level of the nipple divides these two zones, as well as other zones, into upper and lower

It is essential for the accuracy of this method of classification to chart the position of the tumor in the breast with the patient in the supine, *not* in the erect position When the patient sits erect tumors of the lower portion of the breast are obscured by the dependent breast and their exact site cannot be accurately depicted

Other Techniques of Examination

Transillumination of the breast as a diagnostic aid was popularized by Cutler in the 1920 s Some clinicians, such as Huguenin, have found after a thorough

ably for this reason have a poorer prognosis But the available information on this point is inadequate because of the informal way in which the position of tumors in the breast has been recorded in case series In most case records the site of the tumor is described in words by an intern who has not given this question much thought and whose statement is often not specific Quite apart from this inadequacy of the intern, I believe that it is often difficult or impossible to describe the exact position of a breast tumor in words A sketch of the thorax, such as it has been my custom to make when examining patients, is much more

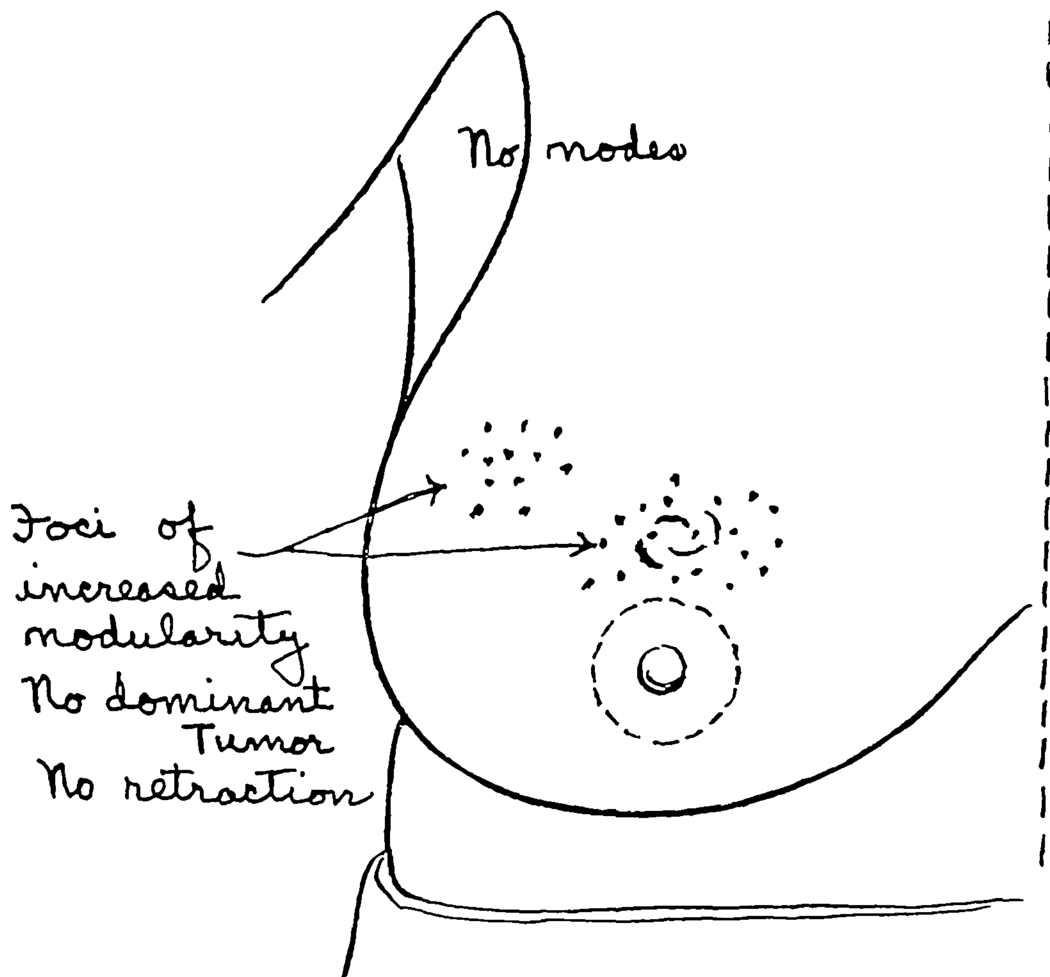


Fig 99 Sketch of the physical findings in a breast with increased nodularity

accurate than a written description It shows the site of the tumor in the individual breast precisely, as well as its relationship to adjacent anatomical features of the thorax From these sketches of mine it has been possible to deduce the site of the carcinoma in the breast with a degree of accuracy not usually attained in case series, and to correlate the relationship of the site of the tumor with its natural history

For those who cannot themselves make a reasonably accurate sketch of the thorax I have included, with my summary sheet, printed stylized drawings of the left and right thorax, showing the patient in the supine position (Figs 102 and 103), upon which the breast tumor can be drawn This method of indicating the site of the tumor is not as good as sketching the individual patient, but it is much more accurate than a written description

trated iodine solution such as *Uroselectan B* as an injection medium and reports that he has had no untoward reactions from it

Sandblom and Löfgren in Sweden have refined the technique of injecting the nipple ducts with a contrast medium and studying them roentgenographically They find the method indispensable for localizing the intraductal lesion in patients with a nipple discharge but no palpable tumor Study of their reported results with the method reveals however that they failed to find a papilloma in 9 of the 20 patients without a palpable tumor in whom they used it

I hesitate to use the intraductal injection method of study in these patients with a nipple discharge In those who have a tumor or a pressure point that

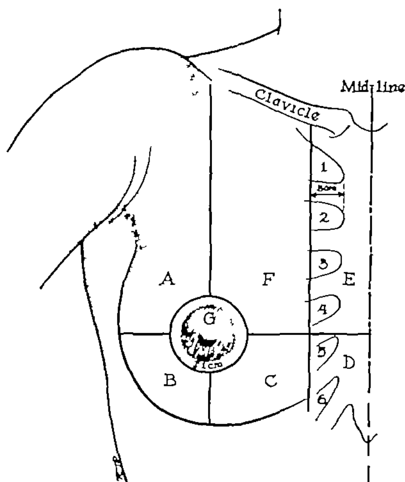


Fig 102. Diagram of the right breast used for indicating the site of the tumor

localizes the lesion intraductal injection is not necessary Surgical exploration can be done at once In the remaining smaller group of patients without localizing signs repeated palpation over a limited period of time, searching for a pressure point seems to me safer In the infrequent carcinoma in this group of cases I would fear that injection of the ducts might produce metastasis The disease is largely intraductal in these cases and injecting the ducts under pressure might force carcinoma cells into blood or lymph vessels. Moreover the information gained by roentgenography of injected ducts is not of decisive diagnostic significance Biopsy again, is the only sure guide to the nature of the lesion. The hazards of intraductal injection to my mind outweigh the value of what may be learned from it

trial, that transillumination is a helpful aid in diagnosis In my own experience I have found it to be of such limited usefulness that I do not employ it A papillary cystadenoma containing bloody fluid, situated in the subareolar area of a dependent breast, will show up well in transillumination as a sharply delimited, entirely opaque shadow But even when it gives this picture, transillumination does not rule out carcinoma, and further diagnostic steps are necessary

Roentgen-ray Examination. The injection of an opaque medium into the duct system of the breast and roentgenographic study—so-called mammography

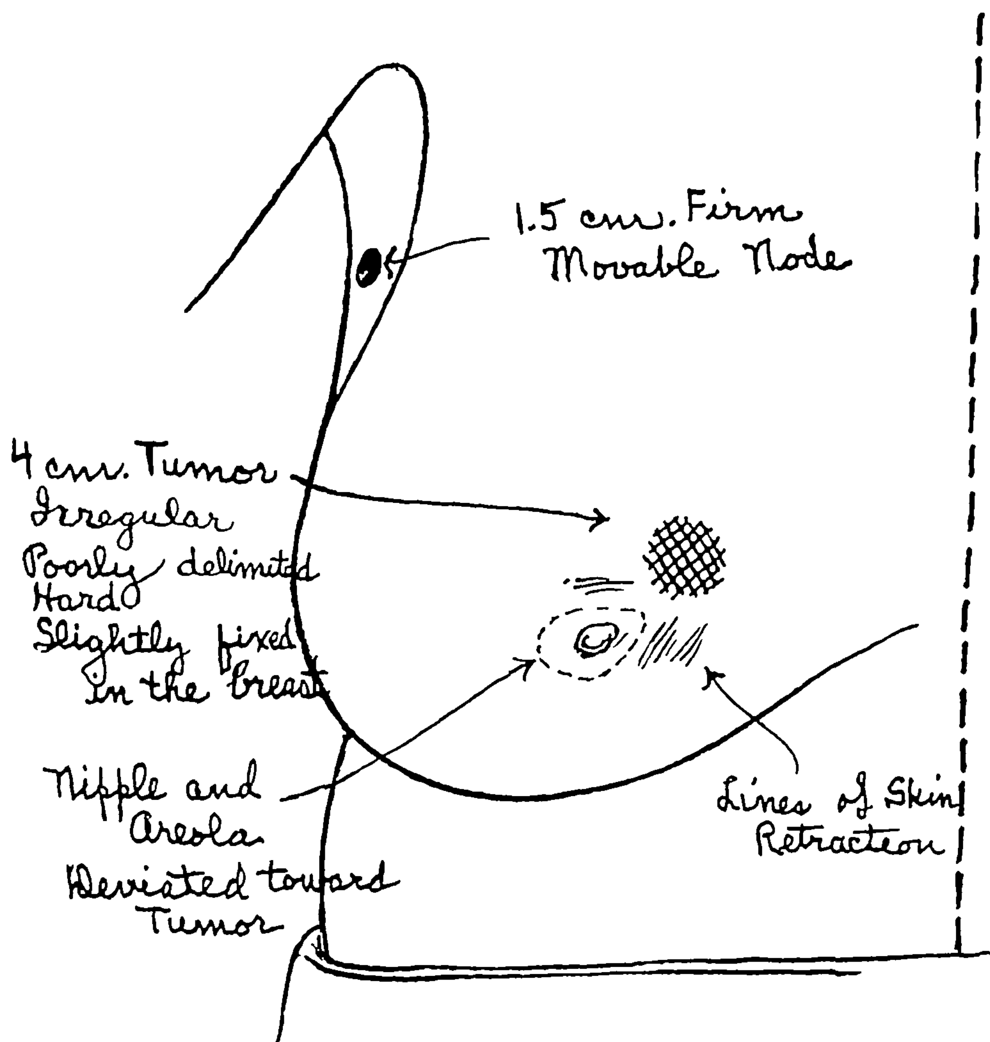


Fig 101 Sketch of the physical findings in a carcinoma of the breast

—was enthusiastically advocated by Hicken and his associates in the 1930's They used colloidal thorium dioxide as a contrast medium Romano and McFetridge, among others, shortly pointed out that the injection of iodized oil or thorium dioxide into the breast ducts not infrequently produced sharp foreign body reactions, and even abscess formation, sometimes necessitating mastectomy This objection has of course now been overcome by the development of harmless contrast mediums

The difficulty in injecting the mammary ducts, however, has kept most of the clinics in our country from taking up the method It is much used in a number of South American clinics, where Leborgne has popularized it He uses a concen-

In our own clinic we have not made roentgenograms of diseased breasts Our point of view has been that even at their best roentgenograms cannot provide decisive information Only biopsies studied microscopically do that Since roentgenograms add to the expense which patients have to bear expense already too heavy we have not thought them to be justified

Isotope Studies Studies of breast carcinoma have been made with several radioactive isotopes, hoping to demonstrate their concentration in tumor tissue McCorkle and Low Beer studied the uptake of radioactive phosphorus in a variety of breast lesions, including carcinoma but were unable to demonstrate differences of diagnostic significance

The Tentative Diagnosis

When the clinical history and the examination of the breast have been completed the physician must decide as best he can whether he is dealing with a harmless physiological condition such as increased nodularity of the breast, or with real disease of the breast For the former nothing is required but reassurance For the latter steps must be taken to prove the presence and nature of the presumed disease There are certain symptoms which are definite indications of disease in the breast, and which it is not safe to ignore They are

1 *A dominant tumor* With certain infrequent exceptions which I will mention in dealing separately with cystic disease, adenosis and so forth a dominant tumor always requires investigation

2. *Marked increase in the size and firmness* of one breast.

3 *Retraction signs* dimpling of the skin distortion of the contour of the breast, decrease in its mobility on the chest wall shrinkage of the breast, narrowing of the areola, deviation of the axis of the nipple, or retraction of the nipple

4 *Redness or edema* of the skin over the breast.

5 *A spontaneous nipple discharge* either serous bloody or watery (except for a bloody discharge during pregnancy)

6 *Erosion* of the epithelium of the surface of the nipple

Having tentatively determined that his patient has breast disease the physician should next try to identify the disease This is still more difficult None of the symptoms and clinical signs that I have mentioned are pathognomonic There are a number of benign lesions of the breast that simulate carcinoma more or less closely—a low grade abscess traumatic fat necrosis duct ectasia, adenosis Any of these may form a hard, poorly delimited tumor of the breast with skin dimpling The circumscribed type of carcinoma, on the other hand, may seem as well delimited as a cyst Nevertheless it is a good intellectual discipline for the examiner to write down his tentative diagnosis when he has completed his history and examination In this way he has a record of his mistake, if subsequent biopsy proves him wrong. On my summary sheet Column 47 is reserved for this purpose.

In the last analysis experience is the only answer to the difficulties of the interpretation of clinical findings in the breast This means experience in the clinical examination of the breast strictly disciplined by accurate pathological study of tissue removed for biopsy and checked by follow up reports of the patient s sub-

The fact that roentgen ray studies of the breast can reveal a good deal of soft tissue detail which can be correlated to a degree with the pathology of breast disease was demonstrated by Stafford Warren in the early 1930's The method was shortly tried out in several clinics, by Vogel in Leipzig, Ritvo in Boston, Lockwood in Kansas City, and Leborgne in Montevideo, but it has never achieved general popularity

In Philadelphia, however, there has been continued interest in the roentgenography of the breast, and a series of careful studies on this subject have appeared from various clinics in that city during the last twenty years Among those

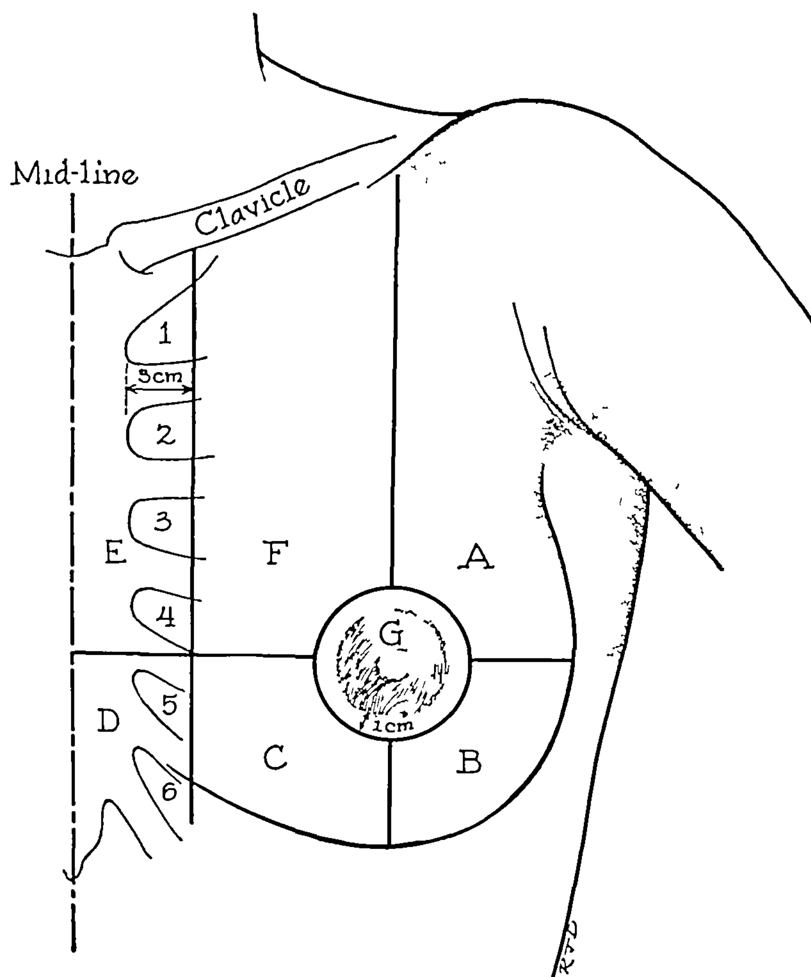


Fig 103 Diagram of the left breast used for indicating the site of the tumor

which should be mentioned are the studies by Seabold, Gershon-Cohen and Strickler, Gershon-Cohen and Hodes, Gershon-Cohen and Ingleby, and Lame and Pendergrass The latter have developed a technique in which the patient stands and bends forward In this position, also advocated by Ehrlich, the breasts fall away from the chest wall and can be viewed from the side

From these studies it is evident that carefully taken roentgenograms will reveal to a considerable degree the soft tissue details of some lesions of the breast Leborgne has pointed out the presence of tiny opacities resembling grains of sand throughout some carcinomas Gricouroff and his associates have demonstrated that these represent calcium in minute areas of necrosis in the carcinoma

may coexist in the breast the cyst or cysts being prominent and the carcinoma small as in Figure 104 Aspiration would empty the cyst but leave the inconspicuous carcinoma undetected Surgical exploration of a case of this kind, with excision of the cyst and careful inspection and palpation of the surrounding breast tissue through the open wound would be more likely to detect the carcinoma.

A final objection to aspiration biopsy is that success with this method becomes more and more difficult as the carcinoma diminishes in size It is difficult indeed to hit with the point of the aspirating needle a nodule located in the depths of the breast and measuring only 4 or 5 mm in diameter Yet as the education of women in the detection of tumors of the breast improves lesions of this size are seen more and more frequently It is just in such difficult diagnoses, when one

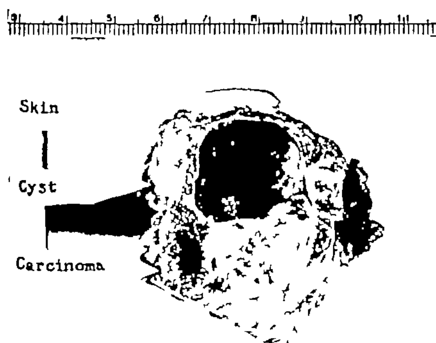


Fig 104 A cyst of the breast masking a carcinoma situated deep to it.

must have a reliable method of proving the nature of the tumor that the aspiration will most often fail We have seen a number of patients in whom aspiration biopsy had been performed by an experienced aspirator a specimen obtained which did not show carcinoma, and a reassuring opinion given yet the subsequent course of events proved that carcinoma was present and had certainly been missed by the aspirating needle In his recent defense of aspiration biopsy Robbins does not discuss the patients whose carcinomas were missed by aspiration biopsy and who subsequently went to other clinics where the correct diagnosis was made by incisional biopsy

Trephine Biopsy When a trephine instead of a needle is used for biopsy it is possible to secure a much better specimen for microscopical study Christiansen at the Copenhagen Radium Centre perfected this method for biopsying soft part tumors, and it has been used in that clinic for biopsying breast tumors since

sequent course For every physician the accumulation of this kind of disciplined experience is an individual educational achievement If he has a good pathologist and a good case record system to help him, and if he has the required intellectual honesty and humility, he will steadily improve in his diagnostic skill

Biopsy Methods

What the patient and surgeon both require, however, is not a tentative diagnosis, but a definitive one The surgeon must have *proof* of the nature of the disease because his therapy is so different for different lesions Benign lesions, in general, require only harmless limited local excision, while carcinoma requires a formidable and mutilating operation that must never be performed needlessly There is no half way therapeutic ground, such as partial or simple mastectomy, in which the surgeon can take refuge in his dilemma *The truth is that the only kind of evidence upon which a surgeon can wholly rely today is microscopical proof* Biopsy therefore should *always* be done before any therapeutic procedure is carried out The only question that needs discussion is the method of obtaining the specimen for microscopical study

Aspiration Biopsy. Aspiration biopsy has been advocated by the Memorial Hospital group for some years and has gained some adherents The procedure is ordinarily carried out in the surgeon's office before the patient has entered the hospital After local anesthesia, a large-bore needle attached to a syringe is inserted into the tumor and, while suction is exerted, is withdrawn and advanced several times, sucking up a core of tumor cells into the bore of the needle The material thus obtained is smeared on a glass slide and fixed and stained In this manner, a fairly accurate impression of the cell types of the tumor is gained, although the details of cell structure are distorted by the crudity of the fixation and staining

Other surgeons have devised a variety of trocars for boring out bits of tissue In this manner, enough tissue may be obtained so that it can be fixed, embedded and cut in the usual way

All such preparations give very little information, however, as to the cellular arrangement and the general architecture of the lesion The pathologist is forced to rely solely on cytology, and usually upon poor cytology This is a great handicap For example, in distinguishing certain better differentiated types of carcinoma of the breast from benign epithelial proliferation, the arrangement of the cells within the ducts, as well as their invasive character, is just as important as the type of cells Aspiration biopsy does not provide this crucial information This is the main reason why Dr Stout and I, working together at this problem over a period of years, have come to believe that aspiration or trocar biopsy is not a reliable method of diagnosing lesions in the breast

There is also a theoretical objection to needle biopsy on the ground of its roughness A good deal of force is required to plunge a large-bore needle into the firm structure of mammary carcinoma—and this is exerted not once but several times We fear that this trauma may squeeze carcinoma emboli into veins If our emphasis on gentleness in manipulating carcinoma of the breast means anything, we should avoid a method as rough as aspiration biopsy

Another disadvantage of aspiration biopsy is that cystic disease and carcinoma

are sometimes seen in which the cells enlarge and develop huge atypical hyper chromatic nuclei, which in smears so closely resemble carcinoma cells that even the most skilled pathologist may be deceived Figure 105 shows such abnormal carcinoma like cells in an area of entirely benign intraductal papillary prolifera tion of the apocrine type Figure 106 shows deceptively carcinoma like cells in a smear of nipple secretion from the breast containing this lesion

Incisional Biopsy We prefer incisional biopsy and frozen section as the method of choice in proving the nature of tumors of the breast. Our procedure is as follows The diagnostic problem is discussed fully with the patient, as gently and as hopefully as possible Her consent is obtained for radical mastectomy should it be required She is admitted to the hospital and all preparations are



Fig 105 Atypical gigantic cells in the apocrine type of benign papillary epithelial proliferation of the breast.

made for the radical operation The surgical pathologist often sees and examines the patient before operation He is regularly present in the operating room when the biopsy is done Intravenous Pentothal sodium supplemented with nitrous oxide and oxygen is our anesthetic of choice We do not use local anesthesia it puts the patient on the rack of suspense while the diagnosis is being made

If the tumor is presumed to be a carcinoma a small incision 3 or 4 cm. in length is made through the skin over it and deepened to expose its surface. If the tumor is thought to be benign the incision is placed as indicated in Chapter 6 All vessels are meticulously caught with mosquito clamps and tied with fine silk so that the wound is perfectly dry and the surgeon is able to see the cut surface of the lesion as he incises it. If the tumor is solid a small wedge measuring about 3 x 5 mm is excised This is ordinarily adequate for our frozen section On in

1939 Kaae has reported that the use of this method of biopsy has not had any unfavorable effect upon the prognosis of breast carcinoma

The objection that trephine biopsy may miss a small carcinoma in the depths of the breast which would be found by incisional biopsy, is one which I must raise Trephine biopsy can scarcely be any more accurate in this regard than needle aspiration biopsy

Intraductal Biopsy. I mention, only to condemn, a method of intraductal biopsy developed by Leborgne in Montevideo He has devised a set of small instruments, dilators and loop curettes, which he inserts through the nipple ducts to reach the lesions and to secure small fragments of them These are sectioned and stained in the usual way

I have already pointed out that *papillary* lesions in the breast are among the most difficult to distinguish as benign or malignant, and that only a full-sized and carefully prepared histological section is adequate I could never venture to diagnose such a lesion from a few minute fragments of tissue secured by Leborgne's method

Smears of Nipple Secretion. Sporadic attempts have been made to make diagnoses from smears of nipple secretions, but with indifferent success Cheatle and Cutler, in their book on breast tumors, were among the first to recommend microscopical study of nipple secretions

Saphir has recently made a careful study of smears of nipple secretion in a series of 90 patients with spontaneous nipple discharge He showed that the study of smears permits the diagnosis of papilloma as well as carcinoma in a considerable proportion of cases, but pointed out that he made some false positive as well as false negative reports

Jackson and his associates have made an extensive study of nipple secretions obtained by *expression* They attempted to express secretion from both breasts of every patient who came with a complaint referable to either breast They make the point that they used only *gentle* pressure, yet they obtained secretion in 77 per cent of the breasts thus examined Although they were able to demonstrate tumor cells in a considerable proportion of patients with intraductal papillomas and carcinomas, they could not differentiate these two lesions from each other by the study of smears Their method therefore cannot be regarded as having much practical value in differential diagnosis Moreover, it seems to me that the danger of causing metastasis by squeezing a breast containing carcinoma is so real that Jackson's procedure should never be used in studying breast lesions

When there is an actual erosion of the nipple due to the Paget's type of carcinoma, it is of course possible to make a smear directly from the erosion and sometimes to demonstrate cancer cells Eisen and Taft have reported such a case In my opinion, however, it is not much more trouble to take a small wedge biopsy of the erosion with the knife, a procedure which has the great advantage of providing a good histological section that will give an unequivocal diagnosis

Papanicolaou and his followers have recently advocated cytological study of nipple discharge (Romberg, Sicard, et al) The disadvantage of smears of nipple secretion is that they may give false positives and lead to errors in diagnosis and treatment In the apocrine type of benign papillary epithelial proliferation, areas

are floated out in a basin of water and picked out on a glass rod and stained in an aqueous polychrome stain Only five or ten minutes are required to prepare these sections

Although we believe that frozen sections made in this manner provide adequate microscopic evidence we have learned that there is one type of neoplasm in the breast in which nothing except a good paraffin section suffices This is the papillary type of neoplasm It is so difficult to distinguish papillary carcinoma from papilloma microscopically that all papillary lesions that are not grossly typical intraductal papillomas should be regarded as too difficult for frozen section diagnosis Preliminary biopsy as a separate operative procedure, and careful study of paraffin sections, should precede any definite operative therapy

There are rare occasions when the frozen section method will fail to give an immediate diagnosis because the microscopic picture is confused by the presence of inflammation or by the variety and richness of the epithelial proliferation The well differentiated carcinomas of course, give the most difficulty On the

Table 10. The Influence of Biopsy on the Results of Radical Mastectomy in Primary Cases (Presbyterian Hospital 1915–1942)

Procedure	Number of operations	5 year local recurrence No	5 year local recurrence Per cent	5 year clinical cures No	5 year clinical cures Per cent
No biopsy	581	133	22 9	188	32 4
Biopsy 6 days or less preoperative	13	1	7 7	11	84 6
7 to 12 days preoperative	14	2	14 3	7	50 0
13 days or more preoperative	35	3	8 6	20	57 2
Biopsy at operation	492	71	14 3	251	51 0
Totals	1135	210	18 5	477	42 0

rare occasions when the pathologist cannot be certain what the lesion is the surgeon closes the wound and waits for paraffin section available in twenty four hours. *He does not proceed with mastectomy without being certain of his diagnosis*

The surgeon who performs a radical mastectomy merely on the suspicion that he is dealing with a carcinoma, because he feels that it is not safe to wait until a definitive diagnosis is made is using poor judgment and may mutilate his patient needlessly A reasonable delay does not apparently prejudice the patient s chance of cure The study of a series of cases of carcinoma of the breast in our clinic in which there was a delay between biopsy and radical mastectomy indicated that the end results were no worse than in cases in which immediate operations were carried out As shown in Table 10 there were a total of 49 cases in this delayed operation group with an interval of more than seven days between biopsy and operation The fact that the results of operation were in fact somewhat better in this group is no doubt merely an indication that diagnostic difficulties requiring delay are more frequent with well differentiated tumors that are as a group less malignant

frequent occasions when the microscopic diagnosis is difficult, the pathologist may ask for a second small wedge of tissue We do not excise the whole tumor for diagnosis unless it is a very small one, measuring only a few millimeters in diameter, for we believe that the practice adds unnecessarily to the risk of producing metastasis If the carcinoma is several centimeters in diameter, the line of local excision around its gross limits will cut across veins and lymphatics of considerable size which may carry off cancer emboli

Excision of the entire tumor for biopsy is, however, the general practice throughout our country Harrington, for example, stated "The tumor should be removed by wide excision, well away from the limits of the growth " Saphir has recently again recommended this procedure The usual argument in favor of this practice is that there is less chance of causing metastasis if the line of excision is around and not through the tumor This reasoning does not have the support of pathology We know that carcinoma frequently infiltrates far beyond the



Fig 106 Deceptively carcinoma-like cells in smear of nipple secretion from breast containing benign intraductal papillary proliferation

grossly visible limits of the disease and that no surgeon can hope that a local excision will get beyond it

Since we cannot avoid cutting through carcinoma whether we incise the tumor and remove a tiny wedge, or excise the tumor as a whole, it seems reasonable to perform the smallest possible procedure which will yield a diagnosis A tiny wedge almost always suffices We have not had the experience that the structure of neoplasms of the breast is apt to differ much in different parts of the tumor It is essential, of course, that the surgeon know enough gross pathology to be able to recognize disease in the breast when he exposes it, and that he have a meticulous enough surgical technique to enable him to keep the biopsy wound dry so that he can see the lesion

The small wedge that we excise for frozen section is heated for a few seconds in Bouin's fixative It is then frozen and cut on a freezing microtome We cut a block of tissue of sufficient size to show the architecture of the tumor We do *not* depend on a section so small that only a few cells are shown The sections

Mammary Carcinoma Summary

Name Date Admitted Unit No

10 STATUS

Y White application slip only
X O P D record only
0 Admitted to hospital
1 Primary case—ward
2 Private
3 Secondary case—ward
4 Private

TREATMENT

5 Limited surgery—date
Hosp
operation
6 Radical operation—date
Hosp
7 Irradiation from to
Hosp
9 *Details of prev treatment not stated*

11 NATIONALITY

Y Native born *of native parentage*
X Native born of foreign parentage
0 Foreign born

National Extraction

1 United States and possessions
2 England, Wales, British colonies
3 Scotland
4 Ireland
5 British Canada
6 Denmark, Norway Sweden, Iceland
7 Germany Holland, Bohemia, Austria, German Switzerland
8 France, Belgium, French Canada, French Switzerland
9 Spain, Mexico Spanish South America

12

Y Portugal Portuguese South America
X Italy Italian Switzerland
0 Poland, Slovakia, Hungary Moravia
1 Balkans, including Yugoslavia and Albania
2 Russia
3 Finland, Esthonia Latvia, Lithuania
4 Turkey Palestine, Mesopotamia
5 Australia, New Zealand
6 American Negro
7 West Indian Negro
8 Mongoloids
9 Miscellaneous

14 AGE years

Y Under 30
X 30–34
0 35–39
1 40–44
2 45–49
3 50–54
4 55–59
5 60–64
6 65–69
7 70–74
8 75 and over
9 Age unknown

15 MARITAL STAGE

Y Single
X Married
0 Widowed
1 Separated or divorced
2 Not stated

AGE AT MARRIAGE years
(*mult.* code)

16 AGE AT FIRST PREGNANCY
years (mult code)

17 NUMBER PREGNANCIES

List of pregnancies in order
No. Year Termination Present age child

18 NUMBER VIABLE BIRTHS

19 NUMBER ABORTIONS

20 MENSTRUAL HISTORY

(Age *at onset* years)
Y Onset 12 or younger
X 13–15
1 16 or older
1 Frequency normal (24–32 days)
2 long (33 days or more)
3 short (23 days or less)
4 Duration normal (3–6 days)
5 long (7 days or more)
6 short (2 days or less)
7 Regular
8 Irregular
9 Menstrual history not stated

Siemens reported a similar experience from the Surgical Clinic of Kiel University In 53 of his patients from 10 to 45 days elapsed between the biopsy and radical mastectomy, yet the cure rate for this group was comparatively high Scheel reports from Oslo that biopsy carried out from one to several days before radical operation had no untoward effect upon the cure rate in a series of 300 consecutive cases

While we do not, of course, recommend delaying operation when it can be done at once, this evidence justifies delay that is unavoidable, as, for instance, when the frozen sections do not yield a definite diagnosis or when a pathologist is not available to prepare frozen sections, and the surgeon has no other course but to excise tissue for biopsy and send it to a pathologist in the community for a twenty-four hour paraffin section

Simple mastectomy as an alternative procedure when the biopsy fails to yield an immediate microscopic diagnosis is, in our opinion, equally unwise If the lesion finally proves to be benign, removal of the breast is unnecessary If it proves to be a carcinoma, a simple mastectomy spoils the field, speaking in a technical sense, for a proper radical mastectomy, besides putting the patient through an additional major operation

To return to the surgeon in the operating room who has just received word from the pathologist that the frozen section shows carcinoma, I recommend that he close his biopsy wound by suturing it tightly with a continuous running suture without disturbing the gauze packing that he left in the wound when he removed his biopsy Since the danger of blood oozing from the biopsy wound and carrying cancer cells into the operative field of the subsequent radical mastectomy is very real, I seal the biopsy wound with a large patch of rubber dam cemented in place with a good cement

Patients with a spontaneous nipple discharge who do not have a palpable tumor present a special diagnostic problem Later, in chapters dealing with intraductal papilloma and with the diagnosis of carcinoma, I shall discuss the technique to be followed in the surgical exploration of these patients

The method that I have described for proving the diagnosis of a tumor of the breast is not only the most reliable one, but it is the one most likely to lead to prompt treatment When the procedure has been explained to the patient, it leaves her in no doubt about the serious possibilities of her seemingly innocuous tumor She is usually willing to come into the hospital at once From the physician's point of view, it provides him with a direct and adequate plan to follow for every patient with a lesion in the breast He will not be tempted to biopsy the tumor in his office If he is not a member of the surgical staff of a reputable hospital or is not himself qualified to perform a radical mastectomy, he will refer the patient immediately to a surgeon who is properly qualified He will not procrastinate because he is in doubt about the nature of the lesion, sending the patient away with instructions to apply heat or cold, or reassuring her and telling her to return after a few months Instead, he will at once send every woman with a dominant tumor in her breast, or retraction signs, or erosion, or abnormal discharge from the nipple, into the hospital to have the nature of her lesion proved by biopsy The practice of this simple rule is the best hope of assuring prompt and correct diagnosis

Mammary Carcinoma Summary—*Continued*

6 Spontaneous discharge from nipple —duration
7 Serous
8 Bloody
9 Other type of nipple discharge—specify

29

Y Axillary tumor—duration
X Swelling of arm—duration
0 Pain in axilla or arm—duration
1 Supraclavicular tumor—duration
2 Dyspnea—duration
3 Cough—duration
4 Pain suggestive of bone metast — site duration
5 Abdominal symptoms—specify duration
6 Neurological symptoms—specify duration
7 Other symptoms—specify duration
8 No symptoms of breast ca. noted by patient before exam. in this clinic —specify clinic making diagnosis
9 Details of present illness unknown

30 DURATION OF SYMPTOMS

(to date of exam in P H) exactly

Y Under 2 weeks
X Between 2 weeks and 1 month
0 1– 2 months
1 3– 5 "
2 6–11 "
3 12–23
4 24–35 "
5 36 months or more
6 Onset during pregnancy
7 Onset during lactation
8 Pregnancy following treatment
9 Duration of symptoms unknown

31 DELAY IN DIAGNOSIS

Y Came to hosp without delay and of own volition
X Came to hosp without delay on advice of M D
0 Delayed by fear of cancer
1 " " economic difficulties
2 " " illness
3 " " negligence
4 " " temporizing advice given by M D
5 Delayed by temporizing advice given by two or more M D
6 Delayed by other causes—specify
7 Improper therapy given while delaying—specify
9 Reason for delay in diagnosis unknown

32 DELAY IN REACHING DIAGNOSIS DUE TO PREV BAD MEDICAL ADVICE

wks.

33 DELAY BETWEEN DIAGNOSIS AND TREATMENT

Y Treatment begun from 1 to 13 days after diagnosis
X from 14–29 days
0 after 30 days
1 Delayed because not summoned by hospital
2 Patient delayed because of unwillingness to accept diagnosis
3 by fear of operation
4 by economic difficulties
5 by illness
6 by negligence
7 on advice of M D
8 other causes—specify
9 Reason for delay between diag and admission unknown

34 DELAY BETWEEN DIAG & ADMISSION TO HOSPITAL days

35 DELAY ON PART OF HOSP IN SUMMONING PATIENT days

36 CLINICAL CHARACTERISTICS OF BREAST LESION

Site

Y Right breast
X Left breast
0 Both breasts involved on adms. (Circle code for first breast involved and write in data for other breast)
1 Upper outer zone—A
2 Lower outer zone—B
3 Lower inner zone—C
4 Lower parasternal zone—D
5 Upper parasternal zone—E
6 Upper inner zone—F
7 Central zone—G
8 Axillary prolongation
9 Description as to site inadequate

Mammary Carcinoma Summary—*Continued*

21	MENOPAUSE (Age at onset)
Y	Not reached
X	39 or younger
0	40 or 41
1	42 or 43
2	44 or 45
3	46 or 47
4	48 or 49
5	50 or 51
6	52 or 53
7	54 or over
9	Menopause history not stated
22	HORMONE THERAPY
Y	None
	Begun Ended Prep Amount
X	Estrogen
0	Corpus luteum
1	Androgen
3	Other hormones
4	X-ray sterilization—date
5	Oophorectomy—date
6	Other gyn oper —date
	Oper
9	Not stated
23	LACTATION HISTORY
Y	Did not nurse any children
X	insufficient milk
0	advised not to nurse
1	prevented by economic or social difficulties
2	Nursed children
	NURSING HISTORY
	Child No Year Nursed Length of Lactation
	Side Child No
3	Non-supp mast (caked br)
4	Abscess—incised
5	Cracked nipple
9	Nursing history not stated
24	FAMILIAL CANCER
Y	None in children, nieces, or nephews
X	in above, spec sib , age, site
0	fate of above unknown
1	None in sisters, brothers, or cousins
2	in above, spec sib , age, site
3	fate of above unknown
4	None in parents, uncles, or aunts
5	in above, spec sib , age, site
6	fate of above unknown
7	None in grandparents
8	in above, spec sib , age, site
9	fate of above unknown

25	PATIENT'S NURSING HISTORY
0	Not nursed
1	Nursed by mother for months
2	no ca of breast in mother
3	ca of breast in mother
4	fate unknown
5	Foster nursed for months
6	no ca of breast in foster nurse
7	ca of breast in foster nurse
8	fate unknown
9	Nursing history unknown
26	PREVIOUS BREAST TUMOR
1	None in either breast
2	Tumor of unknown type in breast
3	Adenofibroma in breast
4	Intraductal papilloma in breast
5	Gross cysts in breast
8	Other condition in breast specify
9	Not stated
27	PRESENT BREAST DISEASE AS NOTED BY PATIENT
Y	Disease discovered by patient herself—specify how
X	Disease discovered by previous examiner
0	Localized tumor—duration
1	No localized tumor noted
2	General hardness—duration
3	Enlargement of breast—duration
4	Shrinkage of breast—duration
5	No pain in breast
6	Pain in breast—duration
7	Tenderness of breast—duration
8	Trauma to breast—specify type and date
9	Ecchymosis (black and blue spot)—duration
28	Redness of skin—duration
Y	Ulceration—duration
X	Edema of skin—duration
0	Skin nodules—duration
1	Dimpling of skin—duration
2	Drawing in of nipple—
3	duration
	Itching or burning of nipple—
4	duration
	Crust or erosion of nipple—
5	duration

Mammary Carcinoma Summary—*Continued*

6 Spontaneous discharge from nipple—duration
7 Serous
8 Bloody
9 Other type of nipple discharge—specify

29

Y Axillary tumor—duration
X Swelling of arm—duration
0 Pain in axilla or arm—duration

1 Supraclavicular tumor—duration

2 Dyspnea—duration
3 Cough—duration
4 Pain suggestive of bone metast.—site duration
5 Abdominal symptoms—specify duration
6 Neurological symptoms—specify duration
7 Other symptoms—specify duration
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(to date of exam. in P H) exactly

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X Between 2 weeks and 1 month
0 1–2 months
1 3–5 "
2 6–11 "
3 12–23 "
4 24–35 "
5 36 months or more
6 Onset during pregnancy
7 Onset during lactation
8 Pregnancy following treatment
9 Duration of symptoms unknown

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X Came to hosp without delay on advice of M D
0 Delayed by fear of cancer
1 " " economic difficulties
2 " " illness
3 " " negligence
4 " " temporizing advice given by M D
5 Delayed by temporizing advice given by two or more M.D
6 Delayed by other causes—specify

7 Improper therapy given while delaying—specify
9 Reason for delay in diagnosis unknown

32 DELAY IN REACHING DIAGNOSIS DUE TO PREV BAD MEDICAL ADVICE

wks.

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0 after 30 days
1 Delayed because not summoned by hospital
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3 by fear of operation
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5 by illness
6 by negligence
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8 other causes—specify
9 Reason for delay between diag and admission unknown

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4 Lower parasternal zone—D
5 Upper parasternal zone—E
6 Upper inner zone—F
7 Central zone—G
8 Axillary prolongation
9 Description as to site inadequate

Mammary Carcinoma Summary—*Continued*

21 MENOPAUSE (Age at onset)
Y Not reached
X 39 or younger
0 40 or 41
1 42 or 43
2 44 or 45
3 46 or 47
4 48 or 49
5 50 or 51
6 52 or 53
7 54 or over
9 Menopause history not stated

22 HORMONE THERAPY
Y None

		Begun	Ended	Prep	Amount
X	Estrogen				
0	Corpus luteum				
1	Androgen				
3	Other hormones				

4 X-ray sterilization—date
5 Oophorectomy—date
6 Other gyn oper —date
Oper
9 Not stated

23 LACTATION HISTORY
Y Did not nurse any children
X insufficient milk
0 advised not to nurse
1 prevented by economic or social difficulties
2 Nursed children

NURSING HISTORY

Child No	Year	Nursed	Length of Lactation

		Side	Child No
3	Non-supp mast (caked br)		
4	Abscess—incised		
5	Cracked nipple		

9 Nursing history not stated

24 FAMILIAL CANCER
Y None in children, nieces, or nephews
X in above, spec sib , age, site
0 fate of above unknown
1 None in sisters, brothers, or cousins
2 in above, spec sib , age, site
3 fate of above unknown
4 None in parents, uncles, or aunts
5 in above, spec sib , age, site
6 fate of above unknown
7 None in grandparents
8 in above, spec sib , age, site
9 fate of above unknown

25 PATIENT'S NURSING HISTORY
0 Not nursed
1 Nursed by mother for months
2 no ca of breast in mother
3 ca of breast in mother
4 fate unknown
5 Foster nursed for months
6 no ca of breast in foster nurse
7 ca of breast in foster nurse
8 fate unknown
9 Nursing history unknown

26 PREVIOUS BREAST TUMOR
1 None in either breast
2 Tumor of unknown type in breast
3 Adenofibroma in breast
4 Intraductal papilloma in breast
5 Gross cysts in breast
8 Other condition in breast specify
9 Not stated

27 PRESENT BREAST DISEASE AS NOTED BY PATIENT
Y Disease discovered by patient herself—specify how
X Disease discovered by previous examiner
0 Localized tumor—duration
1 No localized tumor noted
2 General hardness—duration
3 Enlargement of breast—duration
4 Shrinkage of breast—duration
5 No pain in breast
6 Pain in breast—duration
7 Tenderness of breast—duration
8 Trauma to breast—specify type and date
9 Ecchymosis (black and blue spot)—duration

28 Redness of skin—duration
Y Ulceration—duration
X Edema of skin—duration
0 Skin nodules—duration
1 Dimpling of skin—duration
2 Drawing in of nipple—
3 duration
Itching or burning of nipple—
4 duration
Crust or erosion of nipple—
5 duration

Mammary Carcinoma Summary—*Continued*

1 enlarged
2 called metastasis
3 Supraclavicular nodes not palpable
4 enlarged nodes on homolateral side
5 called metastasis
6 enlarged nodes on contralateral side
7 called metastasis
8 Liver enlarged
9 ascites

46

Y Bone x rays—not made
X negative—bones studied
0 showed metastases in
1 severe anemia—R.B C. HGB.
2 Chest films not made
3 negative
4 showed metastases
5 Parasternal or intercostal tumor—site
7 Contralat. breast metast.—site size
8 Distant skin metast.—site
9 Other metastases—specify

47 CLINICAL CLASSIFICATION—PREOPERATIVE

Y Not carcinoma—specify diag.
X Carcinoma
0 Stage—early
1 moderately advanced
2 far advanced
3 Radical operation indicated
4 not indicated because of advanced state of carcinoma
5 patient constitutionally inoperable—specify why
6 Palliative operation indicated—type
7 Paget's involvement of nipple
8 Inflammatory type
9 Not classified

48 BIOPSY

Y None
X Preoperative—6 days or less
0 7–12 days preoperative
1 13 days or more preoperative
2 in M.D's office or O.P.D
3 At time of operation
4 Extent of biopsy—small wedge from surface of tumor
5 whole tumor excised
6 Apex of axilla
7 Internal mammary nodes excised—interspace
8 Supraclavicular nodes excised

49 OPERATION—date

Y None
X Partial mastectomy
0 Simple mastectomy
1 Simple mastectomy plus axillary dissection
2 Radical mastectomy—pectoralis minor left
3 both pectorals removed
5 thoracodorsal vessels removed
6 " " left
7 " nerve removed
8 " left
9 chest wall resection

50

Y Transverse incision
X Vertical incision
0 Flaps thick
1 Comparatively thin
2 Area of skin removed small
3 comparatively large (meas. cm X cm)
4 Flaps approximated without grafting
5 Plastic flap used to cover defect
6 Thiersch graft
7 Other type of operation—specify
9 Details of operation not stated

51 DURATION OF OPERATION—

exactly min.
1 1– 59 min
2 60–119 "
3 120–179 "
4 180–239
5 240 min or over
9 Duration not stated

52–54 OPERATOR—specify

55 POSTOPER DAYS IN HOSPITAL—

specify days

56 POSTOPERATIVE COMPLICATIONS

Y No complications
X Severe surgical shock
0 Atelectasis
1 Pneumonitis
2 Collection of blood or serum beneath flaps
3 Postoper hemorrhage—serious
4 Wound infection—trivial
5 serious
6 Necrosis of flaps—slight
7 extensive

Mammary Carcinoma Summary—*Continued*

37

0 No tumor palpable
1 Multiple tumors
2 Breast enlarged
3 Breast contracted
4 Breast unchanged in size
5 Breast elevated
6 Breast lowered
7 Breast unchanged in position

38 SIZE—clinical meas
(mm. X mm. X mm.)

1 Greatest diam under 30 mm
2 30–59 mm
3 60–99 mm.
4 100 mm or over
9 Size of tumor not stated

39

Y Sharply delimited tumor
X only moderately well delimited
0 diffuse induration of breast
1 Hard tumor
2 elastic
3 soft
4 cystic
5 Tumor seems to slip about in breast
6 fixed in surrounding mammary tissue
7 No abnorm elevation of breast on pect contract (patient erect)
8 breast abnorm elevated on pect contract (patient erect) (1st degree fixation)

40

Y Breast movable on chest with pect contract (patient supine)
X movability restricted with pect contract (patient supine) (2nd degree fixation)
0 Breast solidly fixed to chest wall (3rd degree fixation)
1 Skin dimpling not demonstrable in any position
2 slight skin dimpling—shown best in position
3 marked skin dimpling
4 skin dimpling at several points
5 No edema of skin
6 edema of limited extent (⅓ or less of skin over breast)
7 wide extent
8 No increased local heat
9 increased local heat

41

Y No redness of skin
X redness of limited extent (⅓ or less of skin over breast)
0 wide extent
1 Skin movable over tumor
2 immovable but not ulcerated
3 ulceration
4 Satellite nodules in skin over breast
5 No dilated veins over breast
6 veins dilated
7 Areola normal in outline and position
8 distorted—describe

42

Y Nipple normal shape
X inverted
0 axis deviated
1 flattened
2 retracted
3 crusted
4 eroded—size erosion mm
5 No discharge from nipple
6 Milky discharge (spontaneous)
7 Serous discharge "
8 Bloody discharge "
9 other type of discharge—specify

43

1 Affected breast otherwise normal
2 nodular and/or cystic
3 Contralateral breast normal
4 nodular and/or cystic
5 Carcinoma—apparently primary—in contralat breast
6 Other findings in breasts—specify
9 No description of tumor

44 CLINICAL EVIDENCES OF METASTASIS

Y Homolateral axillary nodes not palpable
X moderately enlarged (less than 2 5 cm transversely)
0 massively enlarged (2 5 cm or more transversely)
1 soft
2 hard
3 freely movable
4 matted together
5 fixed to deeper structures
6 fixed to overlying skin
7 edema of arm
8 not diagnosed as metastasis
9 called metastasis

45

0 Contralateral axillary nodes not palpable

Mammary Carcinoma Summary—*Continued*

5	Moderately well differentiated
6	Undifferentiated
7	Paget's infiltration of nipple epithelium by tumor
8	Tumor emboli in superficial lymphatics in skin
9	Sections of axillary nodes not available

64	**No. of axillary nodes sectioned**
Y	1– 9
0	10–19
1	20–29
2	30 or more
3	Not recorded
	No of axillary nodes involved
4	none
5	1– 6
6	7–15
7	16–25
8	26 or more
9	all involved

65	
0	Carcinoma in axillary fat
1	Highest axil node not indicated
2	free of carcinoma
3	involved
4	Largest involved axil node less than 1 cm in diam
5	1–1.9 cm.
6	2 cm. or more
7	Internal mammary nodes involved 1st interspace 2nd 3rd
8	Supraclavicular nodes involved
9	Other findings in nodes—specify

66	
Y	No disease in breast tissue other than carcinoma
0	Cystic disease—microscopic
1	Intraductal proliferation of slight degree
2	Intraductal proliferation of marked degree
3	Papillary intraductal proliferation
4	Solid type intraductal proliferation
5	Adenosis
6	Proliferation of medium sized ducts
7	Adenofibroma
8	Other findings—specify

67	**FUNCTIONAL RESULT**
Y	No edema of arm
X	moderate edema of arm
0	marked edema of arm
1	Subsequent attacks of infection in arm
4	Serious radiation damage to skin
5	Lymphangiosarcoma
6	Radiation pneumonitis
7	Other complications—specify
9	Details of clinical result unknown

68	**LOCAL RECURRENCE**
Y	No local recurrence—date examined
X	Local recurrence—exact site unknown—date
0	Recurrence in oper field—chest wall—date
1	in skin of flaps—date
2	in Thiersch graft—date
3	intercostal or parasternal nodule interspace—date
4	treated by surg excis.—date result
5	treated by radiation from to result
6	Recurrence in homolat. axilla—date
7	treated by surg excision—date result
8	treated by radiation from to result
9	Condition of operative field not definitely known

69	**METASTASIS**
Y	No metastasis—date examined
X	Metastasis appeared—exact site unknown—date
0	Lung or pleura—date
1	pleural effusion left right date
2	cough—date
3	Bone metastases—clinical evidence only—date X ray proof date
4	pelvic bones—date
5	lumbar spine—date
6	ribs—date
7	femur—left right date
8	skull—date
9	thoracic spine—date

70	
Y	shoulder girdle—left right date
X	cervical spine—date
0	other bones—specify date
1	Internal mammary metastasis—date
2	Supraclav metast.—homolateral—date

Mammary Carcinoma Summary—*Continued*

8 Other complications—specify

9 Surgical death days postop — cause

57 **PRIMARY RADIATION TREATMENT**

Y None
X Irradiation to breast—begun ended No fields tumor dose r
0 no change or increase in size
1 some regression
2 disappearance of tumor
3 to axilla—begun ended No fields tumor dose r
4 no change or increase in size
5 some regression
6 disappearance of nodes
7 to supraclavicular area—begun ended tumor dose r
8 to internal mammary area—begun ended tumor dose r
9 Details of primary radiation treatment unknown

58 **SUPPLEMENTARY RADIATION TREATMENT**

X None
0 Preoperative irradiation
1 Postoperative prophylactic irradiation
2 Irradiation to recurrences or metastases

		Tr begun	**Tr ended**	**No fields**	**Tumor dose r**
3	Breast or oper field				
4	Axilla				
5	Supraclav				
6	Internal mammary area				
7	Other—specify				

9 Details of supplementary irradiation not stated

59 **SURGICAL PATHOLOGY NO**

Gross Findings

Y Excised skin measured (mm X mm)
X Skin immovable over tumor
0 Erosion of nipple
1 Edema of skin
2 Pectoral fascia involved
3 Pectoral muscle involved
4 Diffuse involvement of whole breast
5 Multiple tumors
6 Tumor papillary
7 Carcinoma circumscribed
8 Mucoid carcinoma
9 Associated gross cystic disease of breast

60 **Tumor measured mm X mm X mm**

0 Greatest diameter under 10 mm
1 10–19 mm
2 20–29 "
3 30–39 "
4 40–49 "
5 50–59 "
6 60–69 "
7 70–79 "
8 80–89 "
9 90 mm or over

61 **No axillary nodes recorded—exactly**

Y No nodes found
X 1– 9 found
0 10–19 "
1 20–29 "
2 30 or more found
3 Number not recorded
Largest ax node measured mm.
4 1– 4 mm
5 5– 9 "
6 10–19 "
7 20–29 "
8 Nodes dissected from specimen
9 cleared

62 **MICROSCOPICAL FINDINGS**

Y Sections of tumor not available
X No special histological type
0 Papillary type
1 Intraductal type
2 Circumscribed type
3 Mucoid type
4 Apocrine type
5 Squamous metaplasia
6 Cartilaginous or osseous metaplasia
9 Other histological type—specify

63

1 Tumor in blood vessels
2 in nerve sheaths
3 in deep lymphatics
4 Well differentiated

Mammary Carcinoma Summary—*Continued*

76	SUMMARY OF FOLLOW UP
Y	5 year survival—breast ca. persisting at end of 5 years
X	7 year survival
0	10 " "
1	15 "
2	20 "
3	25 " "
4	5 year cure—freedom from clinical evid. of breast ca at end of 5 yrs
5	7 year cure
6	10 "
7	15 " "
8	20 " "
9	25 "
77	LENGTH OF SURVIVAL FROM FIRST SYMPTOM months
78	LENGTH OF SURVIVAL FOLLOWING TREATMENT months
79	FINAL CLASSIFICATION AS TO STAGE OF THE *DISEASE*
Y	Limited to breast
X	Breast and homolateral axillary nodes involved (except highest nodes)
0	Apex of axilla involved
1	Internal mammary metastasis
2	Other distant tissues involved—specify
3	Disease operable—early
4	moderately advanced
5	far advanced
6	Disease inoperable Specify grounds (Do not include inoperable patients who have operable tumors)
7	Paget's type
8	Inflammatory type
9	Other type—specify
80	FINAL CLASSIFICATION OF THERAPY GIVEN AT PRESB. HOSPITAL
Y	No radiation or surgery
X	Referred elsewhere—specify reason
0	Refused operation or failed to return
1	Radiation treatment only
2	Local excision of tumor or partial mastectomy only
3	Simple mastectomy only
4	Non-radical surgery plus radiation
5	Internal mammary dissection
6	Radical mastectomy—skin flaps approximated
7	grafted
8	Chest wall resection
9	Other type of operative therapy—specify

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Mammary Carcinoma Summary—*Continued*

3 contralateral—date
4 Intra-abdominal metastasis—exact site unknown—date
5 palpable liver—date
6 ascites—date
7 ovaries—date

71

Y Regional skin metastasis—site date
X en cuirasse—date
0 Distant skin metastasis—site date
1 Contralateral axil metastasis—date
2 Cervical (excepting supraclavicular) metastasis left right date
3 Brain metastasis—date
4 Ocular signs—date
5 Paraplegia—date
6 Other metastasis—specify date
9 Condition as regards metastases unknown

72 **CARCINOMA IN OTHER BREAST**

Y Other breast not involved
X Developed ca in other breast—details unknown—date
0 details known—sector size date
1 Treated by radical surgery—date
2 palliative surgery—type oper date
3 radiation—from to result
4 Axillary nodes not involved—number sectioned
5 number involved
6 Histological type of tumor—specify
7 Classified as primary in other breast
8 Classified as secondary in other breast
9 Condition of other breast not definitely known

73 **TIME OF RECURRENCE OR METASTASIS**

Y Local recurrence—1–11 months
X 12–23 months
0 24–35 "
1 36–47 "
2 48–59 "
3 5 years or over
4 Metastasis—1–11 months
5 12–23 months
6 24–35 "
7 36–47 "
8 48–59 "
9 5 years or over

FOLLOW-UP
(Following sub-classes mutually exclusive except column 75 items 6, 7, 8)

74

Y Lost track of under 5 yrs after treatment—last seen
X Died under 5 years—date
0 operative death
1 cause of death unknown
2 intercurrent disease—no evid persisting of breast ca—specify disease
3 intercurrent disease—breast ca persisting—specify disease
4 from persisting breast carcinoma
5 Alive after 5 years—date last seen
6 without evid breast ca at end of 5 yrs
7 well at end of 5 yrs but recurrence later—date recur
8 breast carcinoma persisting at end of 5 yrs
9 condition unknown

75

Y Died after 5 years—date
X intercurrent disease—no evid persisting breast ca—specify disease
0 intercurrent disease—well at 5 yrs but recurrence later—date recur specify disease
1 from breast ca—well at 5 yrs but recur later—date recur
2 intercurrent disease—breast ca persisting—specify disease
3 from persisting breast ca—original primary
4 from second primary in other breast
5 cause of death unknown
6 Developed carcinoma other than mammary—specify
7 Complete clinical record until shortly before death
8 Autopsy—No Specify metastases

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resultant scars will broaden and are apt to develop keloids Incisions made parallel or in these lines tend to fall together and give hair line scars

Unfortunately Langer did not work out the direction of the lines of skin tension over the female breast, nor have we found a satisfactory description of them from any other source The following Figure 107 is a chart of these lines in the skin over the adult breast as I have determined them

If a tumor is situated near the periphery of the upper part of the breast, far from the areola, at points *A* *B* or *C* it is my custom to make curved incisions

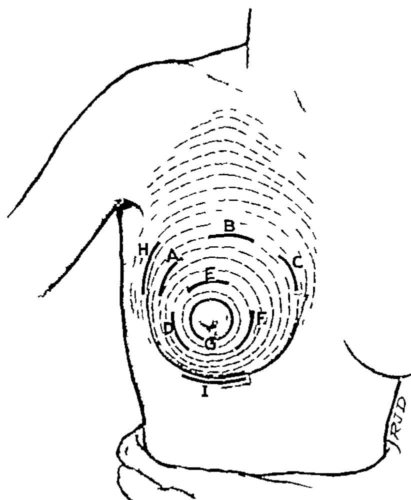


Fig 107 Langer s lines in the skin over the breast.

following Langer s lines and to place them a little medial to the tumor I prefer to place all incisions medial to the tumor if it is at some distance from the center of the breast, as a precaution, should the lesion prove to be a carcinoma It is advantageous to have the biopsy wound as near the center of the operative field as possible in planning the extent of a dissection for carcinoma.

For this same reason I rarely use a lateral paramammary incision as at *H* or an inframammary as at *I* even though these incisions are very convenient for exposing tumors at the periphery of the breast, and even though they give good scars that are hidden from sight by the overlapping breast. If the tumor proves to be a carcinoma the surgeon who has made a paramammary incision

CHAPTER 6

THE TECHNIQUE OF EXCISION OF BENIGN TUMORS OF THE BREAST

A correct technique for the excision of benign tumors of the breast is a matter of great practical surgical importance, because these tumors are so common and because the results of the incorrect technique usually employed are so distressing cosmetically

The surgeon's first duty is, of course, to expose, diagnose, and usually to remove, the lesion, doing as little harm as possible to the breast in the process In keeping with this principle, it is the surgeon's duty to incise and suture the skin in a manner that will give the least visible scar It is desirable to minimize the scar not only because a bad scar is ugly in itself, but because the modern patient, subjected to a good deal of propaganda regarding carcinoma of the breast, is reminded of this unpleasant possibility every time she notices her scar If it is invisible, she avoids a good deal of mental anguish

Unfortunately, a surgical tradition has developed, both in our country and abroad, of making radial incisions in operating upon the breast Nothing could be worse Radial incisions not only produce the worst possible scars, but they are entirely illogical The reason for preferring them which is usually given is that they minimize damage to the ducts In the first place, the ducts in the mature breast may be cut with impunity I have severed all or part of the collecting ducts in many patients without any discernible late after-effects In this regard Davis has reported a follow-up study of 24 patients in whom the ducts beneath the nipple were severed There were no apparent after-effects One patient subsequently bore three children and had no trouble in a breast in which the ducts had been severed In the second place, the direction of the skin incision over the breast need have no relation to the direction of the incision in the breast parenchyma A circular incision through the skin may give access to a radial incision into the breast if that is preferred Personally, I am guided in incising the breast parenchyma only by my desire to find the most direct route through the breast tissue to the tumor

In placing the skin incision, however, great care should be taken to follow the natural lines in the skin, which are the guides to the direction of the normal tension in the skin Langer was the first to trace these lines in detail, and they are usually known as Langer's lines

Incisions through the skin at right angles to these lines will gape, and the

will have great difficulty in keeping his line of dissection sufficiently far away from the biopsy wound which he must assume has been implanted with carcinoma cells I make a paramammary incision only when I am certain the lesion is benign and I cannot often have this degree of confidence in my clinical diagnosis

If a tumor is situated midway between the periphery of the breast and the areola, as at points *D* *E* or *F* and there is some suspicion that it is malignant a curved incision directly over it or slightly medial to it is made If on the other hand the clinical features of the tumor suggest that it is benign a circumareolar incision is used

The circumareolar incision is an exceedingly useful one If correctly placed just inside the edge of the areola, and if it is properly sutured it eventually

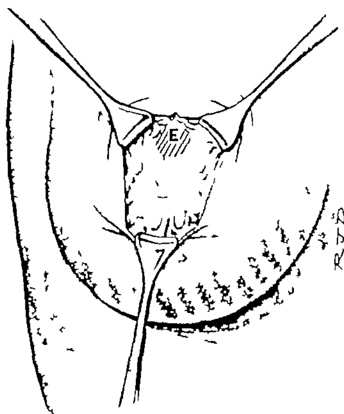


Fig 110 Technique for excising a benign tumor of the breast at some distance from the areola. The tumor at *E* is exposed ready for excision

becomes truly invisible, for the change in the color of the skin hides it. It is the preferred incision for all tumors near the edge of the areola, as at point G and for tumors beneath the areola In using it to expose presumably benign tumors situated some distance out from the edge of the areola it is necessary to undercut a peripheral flap of skin and subcutaneous fat to reach and uncover the tumor

The technique for using a circumareolar incision to expose a benign tumor at some distance from the areola is shown in Figures 108–110 The first step (Fig 108) is to make a marking nick (1) in the edge of the areola at the center of the intended incision This makes it possible to resuture the incision accurately The circumareolar incision (2 3) is then made through the skin around about half of the circumference of the areola. The circumareolar vein will be exposed

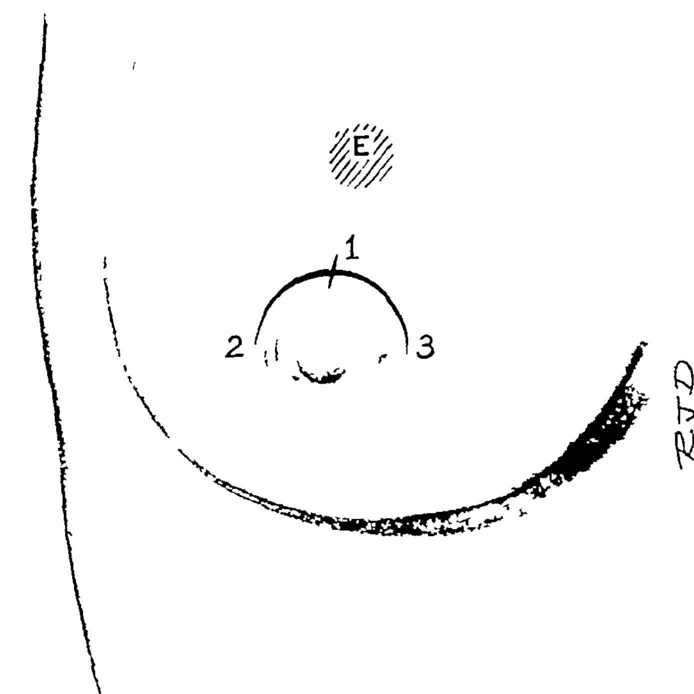


Fig 108 Technique for excising a benign tumor of the breast at some distance from the areola, through a circumareolar incision The incision has been made precisely at the edge of the areola

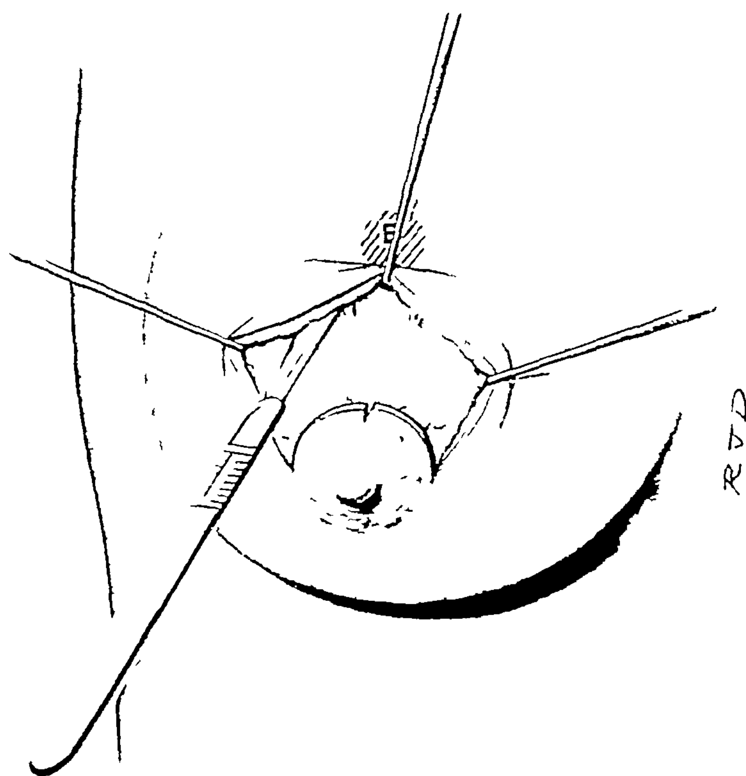


Fig 109 Technique for excising a benign tumor of the breast at some distance from the areola The peripheral flap is being elevated with hooks and undercut

upon the knots and unless tied carefully they will loosen. This subcutaneous layer of sutures helps to keep the scar from widening after the superficial layer of interrupted sutures through the skin itself has been removed a week after operation

I dress these wounds with a few gauze fluffs packed over the operative site, and a six inch elastic Ace bandage applied snugly but not tightly around the chest and fastened with numerous small safety pins No adhesive is used A narrow cloth strap over the shoulder on the operative side holds this brassiere in place I do not dress the wound for a week at which time the supportive Ace bandage is removed and the skin sutures are cut out.

Local excision of a breast tumor carried out according to this plan does not distort the breast. The skin incision is scarcely visible In occasional patients a postoperative hematoma will develop It should be aspirated

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and its branches should be cut, clamped and tied, as required With the aid of skin hooks the peripheral edge of the incision is then elevated, and a flap, indicated by the dotted area, consisting of skin and the subcutaneous fat overlying the breast parenchyma, is dissected up to expose the tumor E (Fig 109) This undercutting can be done with very little or no bleeding if the plane of dissection is kept just above the superficial fascia When the flap has been undercut sufficiently, skin hooks are replaced with three small abdominal retractors to give satisfactory exposure of the breast parenchyma directly overlying the tumor (Fig 110) This is then cut through to reach the tumor

When the tumor has been exposed through an appropriate skin incision, and the wound has been got dry of blood so that it is possible to see the pathology as it is revealed, it is my practice to make a small incision into the lesion If the cut surface seems characteristic of some benign type of tumor such as an adenofibroma, I proceed to excise the tumor, including a narrow rim of the surrounding normal breast parenchyma If inspection of the cut surface leaves any doubt whatever in my mind about the nature of the tumor, I excise only a small wedge, about 5 mm wide and 10 mm in length, to do a frozen section I have had a long experience with the pathology of mammary lesions and am able to recognize some of them from their cut surface with a fair degree of accuracy Surgeons who are less familiar with gross pathology will do well to excise a small wedge for frozen section from every tumor before going ahead with its excision

In excising the various benign lesions of the breast I sacrifice as little of the normal surrounding breast tissue as possible We do not believe that any of the benign lesions of the breast are precancerous in the sense that they are transformed into carcinoma There is therefore no need to remove a wide margin of adjacent breast tissue in order to make certain that the benign lesion is excised in its entirety It is better to leave some remnant of the lesion behind, since it is harmless, rather than to irreparably deform the breast The primary reason for operating upon a benign lesion is to make certain that it is not malignant A secondary purpose is to remove the gross tumor and to restore the breast to as normal a condition as possible—not to ruin it

The lesion having been excised, I search the wound meticulously for bleeding vessels, and clamp and tie them with fine silk I do not drain these wounds, preferring to devote a little extra time to achieving good hemostasis

I have learned not to attempt to suture the breast parenchyma together in an effort to obliterate dead space after excising a tumor No matter how carefully such deep sutures are placed, they deform the breast This is due to its mobility Sutures placed seemingly correctly in the breast flattened out on the chest wall as the patient lies supine on the operating table, will prove to be wrongly placed and to cause distortion of the breast when the patient is erect and the breast is dependent

All incisions through the skin over the breast should be closed with two layers of interrupted sutures I use No 00000 silk on small curved cutting needles (eye needles) The deeper layer of sutures is placed through the subcuticular tissue When used for a circumareolar incision, these sutures also include the areolar muscle The knots on these sutures must be tied precisely and tightly Lying as they do just beneath the skin, the ends of the sutures must be cut flush

which lesions are to be included under the complex of *cystic disease* for a com plex it certainly is I include all the individual benign pathological states that taken together constitute the disease—dilatation of ducts and acini to form cysts, proliferation and metaplasia of their lining epithelium and multiplication of ducts and acini to give the picture of adenosis The cysts may be so small as to be visible only microscopically or large enough to be grossly visible (1 or 2 mm or more) All types of benign proliferation of the lining epithelium of the cysts are included whether apocrine papillary or solid I exclude from the com plex of cystic disease, however three types of lesions which are distinct and characteristic clinical entities and should therefore be carefully distinguished from cystic disease They are

1 Localized adenosis forming a tumor
2. Intraductal papilloma
3 Ectasia of the ducts.

I shall discuss these lesions individually in separate chapters

Frequency

Cystic disease is certainly the most frequent lesion of the breast. Even when only those patients in whom the disease forms cysts large enough to be evident clinically are considered—and this does not include the large group of women who have smaller breast cysts which escape detection—cystic disease exceeds in frequency all other breast lesions. During the ten year period 1941–1950 a total of 1196 patients with clinically evident cystic disease were in the Presbyterian Hospital During the same period 991 patients with breast carcinoma and 440 patients with adenofibroma of the breast were seen

We know that in the state of New York today about one woman in twenty five develops breast carcinoma during her lifetime. Using our data as to the compara tive frequency of clinically evident cystic disease and carcinoma in surgical material we may argue that somewhat more than one woman in twenty develops clinically evident cystic disease before she is past the menopause

The study of the breasts at autopsy has shown however that the true fre- quency of cystic disease is much greater than its clinical incidence There have been several recent studies of this kind based upon a reasonably large number of autopsies Borchardt and Jaffé in 1932 reported that they found microscopical cystic disease in 93 per cent of a series of 100 women over the age of 40 without clinical evidence of mammary disease In 1936 Franzas studied the breasts in 100 necropsies of women between 19 and 80 years of age and found microscopic cystic disease in 55 per cent The disease was bilateral in 25 per cent of the subjects.

Frantz and her associates in 1951 reported a study of the breasts in 225 autopsies of women without clinical evidence of mammary disease. Grossly evident cystic disease (cysts of 1–2 mm or more) was found in 19 per cent In one half of these cases the grossly evident disease was bilateral An additional 34 per cent of Frantz s cases showed microscopic evidence of cystic disease i e microcysts intraductal epithelial proliferation or apocrine metaplasia of the duct epithelium In summary Frantz found the cystic disease complex present in somewhat more than one half (53) of the subjects whom she studied

CHAPTER 7

CYSTIC DISEASE OF THE BREAST

For more than a century, since the time that the English surgeons Astley Cooper and Benjamin Brodie wrote of cystic disease of the breast, it has been recognized as the common benign lesion of the breast developing during middle age The relationship of cystic disease to carcinoma has long been questioned, and it is still debated today This makes cystic disease a subject worthy of thorough discussion

The first comprehensive clinical and pathological descriptions of cystic disease were written in France in the 1880's by Reclus and by Brissaud Reclus' descriptions were so complete that in France, particularly, cystic disease has since borne his name Reclus recognized the multiplicity of the cysts and the fact that both breasts are usually involved by the disease

German surgeons turned their attention to cystic disease in the 1890's Schimmelbusch discussed the disease in detail and it has since been called by his name in Germany Konig wrote of the disease in 1893, and believing it to be inflammatory in origin, called it *chronic cystic mastitis* This name has been widely adopted, and remains one of the important handicaps to our understanding of the disease, for it leads to the false assumption that it is indeed inflammatory

The most comprehensive study of cystic disease that has appeared recently is Semb's monograph based upon a review of 144 surgical cases and 32 autopsies from the University of Oslo Semb was chiefly concerned with the problem of the relationship of cystic disease to carcinoma, and in my discussion of this question I will deal in detail with his findings

Definition

I prefer the simple term *cystic disease* for the lesion under discussion The adjective *chronic*, while certainly expressing a truth regarding the natural history of the disease, makes the name unnecessarily complex Cheatle's name "cystiphorous desquamative epithelial hyperplasia" is the ultimate of prolixity In the Scandinavian countries cystic disease is called "fibroadenomatosis " This is an unfortunate choice because it suggests to us the entirely different lesion, fibroadenoma

We should avoid the term *mastitis* because there is no evidence to suggest that cystic disease is inflammatory in origin

It is also necessary to define, in terms of gross and microscopical pathology,

four whose tumors were discovered after the menopause Two of these patients were 60 and the other two 67 and 69 years of age respectively All four had comparatively small cysts situated in the central area of the breasts Although these four women had discovered their tumors shortly before they came for treatment, I suspect that the tumors may have been present but undiscovered since pre-menopausal time

Chart 1 shows the age distribution in 458 ward and private patients with gross cysts proved by operation in the Presbyterian Hospital between 1930 and 1943 The median age of these patients was 41

Clinically evident cystic disease is therefore a disease of middle aged women as compared with adenofibroma which is a disease of young women Unlike carcinoma of the breast which continues to increase in frequency with advancing age throughout the remaining life span cystic disease sharply diminishes after the menopause

Racial Predilection

Only 10 per cent of our patients with gross cysts of the breast coming to the Presbyterian Hospital between 1930 and 1943 were colored, as compared with 26 5 per cent of colored patients with adenofibroma of the breast. During this period about 15 per cent of all our female patients were colored women It would appear from these data that there is no special racial predilection for the disease

Multiplicity

Grossly visible cysts of the breasts are often multiple In a series of 205 ward patients with the disease coming to the Presbyterian Hospital between 1930 and 1943 (Table 11) *two-thirds had more than one cyst, and 13 per cent had both* breasts involved

Table 11. 205 Ward Patients First Admission for Gross Cysts Proved by Operation
(Presbyterian Hospital 1930–1943)

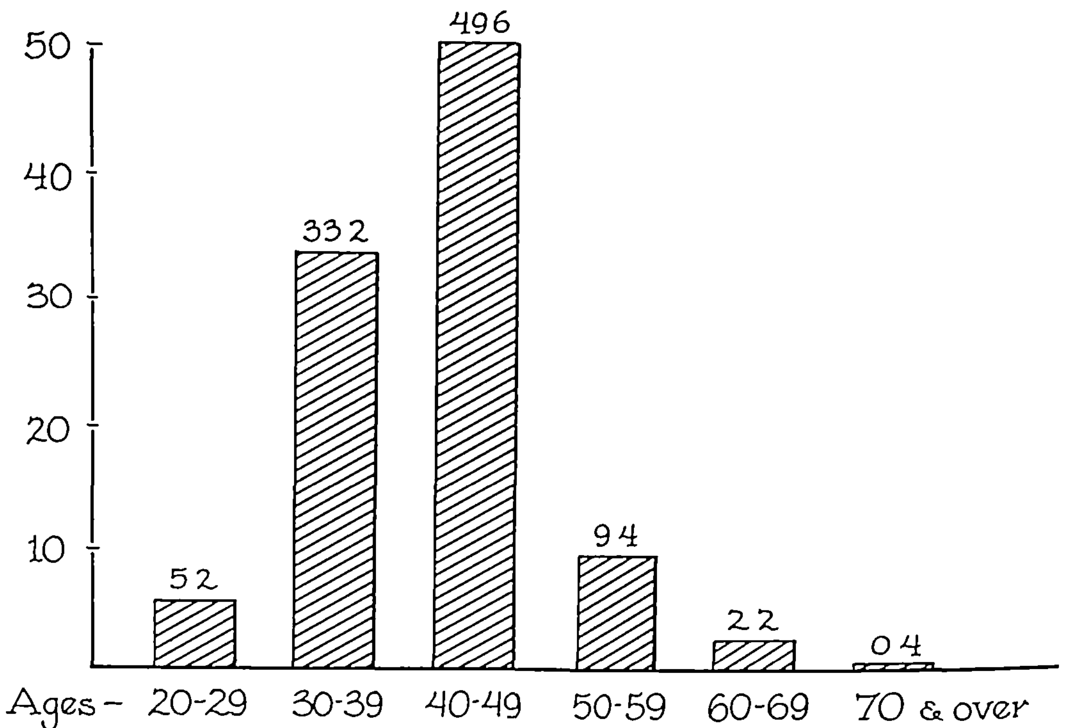
	Number	Per cent
Simple cyst	61	29 8
Multiple cysts	144	70 2
One breast involved	178	86 8
Both breasts involved	27	13 2

These data refer only to the multiplicity of grossly visible cysts at the first admission of the patient If we consider multiplicity of cysts in terms of subsequent new cysts the figure is considerably increased. One third of the patients in our series had subsequent clinically evident new cysts In two-thirds of these patients with new cysts the opposite breast was involved

Etiology

The fact that cystic disease becomes clinically evident in middle life when ovarian function has been at peak level for some years, and that it is unusual for

Kiaer has recently described his findings in 700 breasts studied at autopsy of 350 women with clinically normal breasts He reports finding microscopical "fibroadenomatosis" (i e cystic disease) in 33 per cent Kiaer's definition of the cystic disease complex is a remarkably broad one, including such features as mere variation in the size and shape of the lobules, and increase in the density of the intralobular connective tissue It is therefore difficult to compare his findings with those of Frantz, whose concept of cystic disease is the same as ours Kiaer also failed to state how often he found gross cysts in his series of cases, an omission of fundamental importance because gross cysts are the only evidence of the existence of cystic disease that we can recognize clinically The demonstration



Percentage distribution of ages in 458 patients at first admission for gross cysts proved by operation

Chart 1

of an association between carcinoma and microscopic cystic disease is of no help to us in a practical sense because microscopic cysts provide no clinical evidence of their presence All our subsequent discussion of the problem of cystic disease is therefore focused upon the significance of grossly visible, clinically evident, cysts of the breast

Age Distribution

Clinically evident cystic disease usually makes its appearance during the third decade of life, and reaches its greatest frequency during the fourth decade It is infrequent after the menopause In a series of 205 ward patients with the disease coming to the Presbyterian Hospital between 1930 and 1943, there were only

a period of more than 30 years to date seems to be less than in the same number of women in the same age period who have been operated upon either for lesions outside the breast or for benign lesions of the breast—chiefly encapsulated adenoma—in which the breast showed no evidence of chronic cystic mastitis or the blue-domed cyst

Geschickter continuing the study of the same Johns Hopkins Hospital data reported in the second edition of his book (1945) that among a total of 378 patients followed for from 5 to 30 years, four developed carcinoma Careful reading of Geschickter s cases, however reveals that only two (Case Nos 2 and 3) are valid examples of proved cystic disease followed some years later by carcinoma.

Lewison and Lyons have recently reported a more detailed study of the same Johns Hopkins data. They achieved an 85 per cent follow up One hundred and fifty three patients with cystic disease were followed for an average of 13 3 years In 97 per cent of these the follow up was for more than 5 years, and in 77 per cent it was for more than 10 years Four (2 6 per cent) of these patients developed carcinoma. The details of these cases are not presented

Comparing this incidence of carcinoma in their group of patients with cystic disease, with an estimated attack rate for breast carcinoma among white women in the general population worked out by Dublin Lewison and Lyons concluded that in patients with cystic disease carcinoma occurred in 3 6 times the expected rate.

Johnson (1925) traced 68 patients with cystic disease of the breast for from 1 to 20 years after diagnosis Carcinoma of the breast subsequently developed in only 2.

Campbell in 1934 reported a follow up study of a total of 290 patients with cystic disease from the University of Minnesota Hospital The follow up period was from two to fourteen years 60 4 per cent were followed for five years or longer but only 15 9 per cent for ten years or more Two patients (0 7 per cent) developed carcinoma

Warren s study (1940) of the incidence of breast carcinoma in women who had been previously operated upon for chronic mastitis led him to conclude that this condition predisposes to breast carcinoma. The breast cancer rate for these women according to his calculations was 4 5 times as great as for all women and this predominance was especially marked in the decades below 50 years Warren advised that patients in whom these lesions (chronic mastitis) are found at operation should subsequently be carefully watched and simple mastectomy done if nodules or cysts develop in residual breast tissue " Warren s paper attracted much attention and his advocacy of simple mastectomy for recurrent cysts has resulted in the sacrifice of countless breasts

Warren s evidence consisted of a follow up of a total of 1044 women with "chronic mastitis or chronic cystic mastitis " These cases represented those selected and successfully followed from some 3100 patients coming to various Boston hospitals and to the Toronto General Hospital with various non malignant lesions of the breast The length of follow up was from five to twenty one years for those who did not develop carcinoma with an average length of nine years It is important to note in considering Warren s data that in a con

new cysts to appear after the menopause, suggests that ovarian hormones are in some way concerned with the causation of the disease

The French were pioneers in the experimental study of the effects of the ovarian hormones upon the breast in mice, and one of the earliest papers was that by Goormaghtigh and Amerlinck (1930) in which they reported that they had reproduced cystic disease by the injection of estrogen in ovariectomized mice

As the knowledge of the effects of the ovarian hormones upon the mouse breast evolved from studies carried on in many laboratories, it became evident that estrogen not only stimulates the mammary epithelium to proliferate, but that it also causes dilatation of the mammary ducts and cyst formation The latter process as seen in the mouse breast is similar in a general way to cystic disease in the human breast except that in mice the changes usually involve the whole extent of the mammary gland, while in a considerable proportion of women with cystic disease the changes are to some extent localized

There are marked differences among different strains of mice in this tendency to develop cystic changes following estrogen administration In a study carried out by Randall and myself (1942) in which we used three pure-bred strains of mice—the Paris R 3 strain, the Marsh strain, and the C 57 strain—this fact was well shown The breasts of the Paris R 3 mice showed a great degree of epithelial proliferation accompanied by considerable cystic change The breasts of the Marsh and C 57 mice showed little epithelial proliferation but very marked cystic change In the C 57 mice, in particular, the breasts were transformed into masses of cysts by long continued administration of estrogen in large dosage

Engle, Krakower and I treated a group of aged Rhesus monkeys with estrogen and produced cystic changes in the mammary gland but no epithelial proliferation

The Relationship of Cystic Disease to Carcinoma of the Breast

No question is of more acute concern to the clinician dealing with breast disease than the relationship of grossly visible cysts to carcinoma It is a problem which he must often face and for which the published evidence is confused and conflicting

The Frequency with which Carcinoma Develops Subsequent to Gross Cysts of the Breast. There is first of all the evidence of clinicians who have attempted to find an answer to the question by following their patients who have been operated upon and in whom the presence of gross cysts has been proved In this manner they can determine the incidence of carcinoma of the breast *subsequent* to proved cystic disease Unfortunately the evidence which they present is usually not sufficiently detailed or adequately controlled to permit any very definite conclusions, but it is worth reviewing simply as an indication of what evidence is available

Bloodgood was one of the first to follow such a group of cases of cystic disease His long experience with breast disease left him with a strong impression that cystic disease does not predispose to carcinoma He stated (1929) "When the very large group of patients are followed who have been operated upon for a blue-domed cyst and still have one or both breasts, the incidence of cancer over

a period of more than 30 years to date seems to be less than in the same number of women in the same age period who have been operated upon either for lesions outside the breast or for benign lesions of the breast—chiefly encapsulated adenoma—in which the breast showed no evidence of chronic cystic mastitis or the blue-domed cyst.

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siderable proportion of the patients who developed carcinoma subsequent to an operation for cystic disease, the carcinoma was diagnosed within a relatively short period of time after the operation Warren unfortunately does not include the details of these cases but states that 13 of those who developed cancer were followed "an average of 2 7 years" My own clinical experience makes me suspect that when carcinoma of the breast is diagnosed within a year or two following an operation for a benign lesion, the carcinoma was probably already present—coexisting with cystic disease—at the time of the original operation, and the surgeon missed it This may well have happened in some of Warren's cases— they were collected from a number of hospitals, with a large number of surgeons of varying skill concerned

Clagett and his associates (1944) reported a follow-up study of 183 patients with cystic disease followed for "five to six years" Six (3 3 per cent) of the patients developed carcinoma during this period This is an incidence 10 times as high as their estimated carcinoma attack rate in the general population in Minnesota in 1940 Clagett and his associates give no explanation for the incongruity of their findings—they merely conclude that patients with cystic disease should be closely followed

Patey and Nurick, from the Middlesex Hospital in London, have recently (1953) reported the follow-up of 65 cases of cystic disease from one to sixteen years after treatment by aspiration Only one patient developed carcinoma

Kiaer, in his recent monograph, reported that among 321 patients with proved "fibroadenomatosis" 6 5 per cent developed breast carcinoma during the subsequent follow-up period The period of follow-up was a fairly long one, averaging seventeen years in one group of 231 of Kiaer's patients and 11 7 years in his other group of 90 patients Seventeen of the carcinomas developed in the breast in which the cystic disease had originally occurred, only three developing in the contralateral breast The statistical significance of Kaier's findings was studied by Nielsen He concluded that the incidence of breast carcinoma was higher than expected—21 cases instead of the expected 4 9 cases The opposite breast, in which the original cystic disease had not been diagnosed, did not share the increased expectancy of carcinoma

Satisfactory data bearing upon the incidence of carcinoma of the breast *subsequent* to the demonstration of gross cysts at operation should meet several requirements, among which the following are the most important

1 The data should be obtained from a hospital where adequate clinical histories and careful pathological study of the surgical material have been available

2 Cystic disease should be defined as the complex including *grossly visible cysts*, as well as the microscopic cysts and the various types of epithelial proliferation and metaplasia, and duct and acinar multiplication, usually associated with them Other benign diseases of the breast—*adenofibroma, adenosis, fibrous disease, intraductal papilloma*, and *ectasia of the ducts*—should not be included

3 The total number of ward patients with cystic disease, thus defined, who were operated upon and the presence of the disease proved pathologically, during a specified period of years, should be stated, as well as the type of operation performed

4 The number of this group of patients operated upon and successfully followed in subsequent years with regard to the status of their breast disease should be stated The proportion of patients followed probably has an important bearing upon the reported incidence of subsequent carcinoma. In general the women whose cystic disease gives them no further trouble subsequent to the original operation tend to be lost to follow up But most of those who subsequently develop carcinoma probably return to the clinic where they were originally treated for their breast disease If the proportion of patients followed is low the incidence of subsequent carcinoma therefore appears to be relatively high. The report by Clagett and his associates from the Mayo Clinic is a good example of this fallacy

5 The length of follow up should be stated in detail that is, the percentage of the total number followed for a minimum of five years, ten years etc The data should include at least a ten year follow up of a significant number of patients—a hundred or more

6 For each of the patients who developed carcinoma of the breast subsequent to operation at which gross cysts were found at least the bare details of the case history should be presented, certainly including the interval which elapsed between the operation for cystic disease and the diagnosis of carcinoma

Few of the studies of the incidence of carcinoma *subsequent* to clinically evident gross cysts meet these requirements, and the conclusions which may be drawn from them are limited. Lewison and Lyons study perhaps comes closest to the ideal we have set.

Presbyterian Hospital Data Regarding Breast Carcinoma Subsequent to Clinically Evident Cystic Disease We have for some years, conducted a special follow up clinic in the Presbyterian Hospital for ward patients who have been operated upon and in whom grossly visible cysts were demonstrated. Adequate clinical histories and careful pathological studies of the surgical specimens under Dr Stout s direction have been available for all of these cases. The ten year follow up data for the patients treated during the period 1930 to 1943 can now be reviewed. The private cases had to be excluded from the study because the private follow up has been entirely inadequate

A total of 205 ward patients with clinically evident cystic disease were operated upon during this period Five of these patients had bilateral simple mastectomy because of the extensiveness of the cystic disease In a study of the relationship of cystic disease to the development of carcinoma these patients in whom all breast tissue had been removed must, of course be excluded.

Four of the patients had unilateral simple mastectomy This should reduce the patient s chance of subsequently developing breast carcinoma by no more than one-half since in our series of cases carcinoma occurred, when it did develop as often in the opposite breast as in the breast affected by cystic disease We have therefore included in our analysis these patients in whom one breast was removed The remaining patients in our series were treated by local excision of the cystic portion of the breast.

We have been able to follow 163 or 81 5 per cent of our 200 patients for at

least five years A ten year or more follow-up was achieved for 147, or 73 5 per cent, of the group Carcinoma developed in 8 of these patients, as shown in Table 12

Table 12 Occurrence of Carcinoma of the Breast Following Gross Cysts of Breast Proved by Operation
(Presbyterian Hospital 1930–43)

Number of patients with cysts	Developed carcinoma		Within 10 years	After 10 years
200	4	In same breast	1	3
	4	In opposite breast	3	1

The shortest interval between the original diagnosis of cystic disease and the diagnosis of carcinoma in our series of cases was seven and one-half years The longest interval was sixteen years

The case histories of the eight patients who subsequently developed carcinoma are summarized as follows

Case No. 1. M S , a 39 year old housewife, was admitted to the Westfield State Sanitorium, Westfield, Mass , on 11/26/39, with a movable, 2 cm tumor of the left breast It was excised and proved to be a cyst Two years later, on 9/6/41, she was admitted to the Presbyterian Hospital with a 6 cm , freely movable tumor of the upper outer sector of the same breast It was explored surgically and proved to be another cyst, without any evidence of malignant change

At follow-up examination 10/28/47, a new 1 cm tumor was discovered in the vicinity of the scar of the last operation in the left breast On 4/23/48 this new nodule was biopsied The breast tissue was everywhere riddled with small cysts It was decided to perform a simple mastectomy To everyone's surprise a very small area of intraductal carcinoma was found, in addition to cystic disease generalized throughout the breast On 5/6/48 a simple mastectomy of the right breast was done The breast showed generalized cystic disease but no carcinoma She was last seen 4/5/53, without evidence of recurrence

Case No 2 I M , a 46 year old Negro housewife, came to the Presbyterian Hospita 1/5/42 complaining of a tumor of the right breast of three weeks' duration The tumor was firm but movable, measured 3 x 5 cm , and was situated in the upper outer sector of the breast At operation 1/21/42 it was found to be a group of typical blue-domed cysts which were excised

On 8/6/51 she returned, complaining of a painful tumor of three weeks' duration in the left breast Examination showed a far advanced and inoperable carcinoma of this breast The tumor measured 11 x 8 cm , there was extensive edema of the skin, and axillary lymph nodes measuring 3 cm in transverse diameter The tumor was biopsied, found to be a carcinoma, and she was treated with irradiation She died with liver metastases 11/29/51

Case No. 3 G G , a 47 year old housewife, was admitted to the Presbyterian Hospital on 2/2/39, with a freely movable tumor of the right breast, situated just lateral to the areola At operation 2/3/39 it proved to be a simple cyst without any malignant changes, and was excised

On 7/3/48 she was again admitted to the hospital with a new tumor of the right breast It was situated in the upper outer sector near the periphery of the breast,

measured 7 cm. in diameter and had the characteristics of a carcinoma. At operation on 7/8/48 it was found to be such and radical mastectomy was done In addition to the carcinoma the breast showed generalized cystic disease. Three of 30 axillary nodes contained metastases. The patient developed pleural, spinal and liver metastases, and died 1/4/52.

Case No 4 A O a 30 year old housewife, whose mother had died of carcinoma of the breast at the age of 77 came to the Presbyterian Hospital 8/13/31 complaining of a tumor of the left breast that she had had for ten years It had increased in size during the past year It was situated in the upper outer sector of the breast, measured 2.5 cm. in diameter and was freely movable At exploration 8/15/31 it proved to be a group of cysts without any evidence of carcinoma.

On 7/22/37 she was again admitted to the hospital and another cyst was excised from the left breast in the region of the scar of the previous operation.

On 10/21/42 she was admitted for a third time with a 2.5 cm. tumor near the center of the left breast. At operation on 10/28/42 frozen section showed only epithelial proliferation, but no carcinoma Simple mastectomy was nevertheless done. There were no gross cysts in the amputated breast, but permanent sections showed the tumor to be carcinoma. She was reoperated upon 11/12/42 and the pectoral muscles and axillary contents excised No metastases were found in the axillary nodes She had no evidence of recurrence when last seen 6/26/51 but died of cancer 1/13/52.

Case No 5 E. P a Polish housewife aged 40 came to the Presbyterian Hospital 9/1/32, complaining of a tumor of the left breast of 10 days duration. It was a movable, 3 cm. tumor situated just above the areola At operation on 9/15/32 it proved to be a simple cyst.

She came back to the hospital 3/29/39 complaining of a new tumor in the right breast, of two weeks duration. It was situated just above the areola and measured 5 cm in diameter At operation 3/3/39 it proved to be another simple cyst.

She returned again 1/10/40 with a new tumor 2 cm in diameter in the lower outer sector of the right breast. It had the clinical characteristics of a carcinoma and at operation 1/23/40 it was proved to be one Radical mastectomy was done The carcinoma measured 3 5 cm in diameter The breast was riddled with cysts. Twelve of the 17 axillary lymph nodes, including the highest one, contained metastases She developed local recurrence and liver metastases and died 1/12/41

Case No 6 C L. an unmarried Scottish children s nurse aged 41 was admitted to the Presbyterian Hospital 2/13/36 with a tumor of the right breast of 2 months duration. It was 5 cm. in diameter movable, and situated in the upper inner sector of the breast. At operation a group of simple cysts was found and excised.

On 5/15/50 she was again admitted to the hospital. She had noted a new tumor in the right breast two months previously It was situated in the lower outer sector of the breast, measured 5 cm in diameter and had the characteristics of a carcinoma. At biopsy it was found to be one and radical mastectomy was done. No cysts were found in the amputated breast. Two of nine axillary nodes contained metastases In October 1953 she developed pulmonary metastases which responded well to estrogen.

Case No 7 V O a Negro housewife aged 37 came to the Presbyterian Hospital 3/2/32 complaining of a tumor of the left breast of four months duration. It was situated in the upper inner sector of the breast and was freely movable It measured 3 cm. in diameter At operation 3/29/32 a group of gross cysts was found and excised.

She was again admitted to the hospital on 6/13/40 with a tumor of the right breast of one month s duration It was situated just above the right nipple, was round and movable and measured 3 cm. in diameter At operation 8/2/40 it proved to be a simple cyst without any evidence of malignant change.

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Her third admission for breast disease was 6/30/48 She came in because she had developed a thin yellowish discharge from the right nipple and a new tumor in this breast There was an 8 cm mass with the characteristics of carcinoma in the upper central right breast, and enlarged firm axillary nodes Biopsy confirmed this diagnosis Because the patient had advanced Laennec's cirrhosis, her breast carcinoma was treated with irradiation She died with pulmonary metastases 11/13/48

Case No. 8. E F , a 48 year old housewife, came to the Presbyterian Hospital 4/11/39 complaining of a tumor in the left breast of three weeks' duration The tumor was situated just above and medial to the areola, measured 3 cm in diameter, and was rounded and freely movable At operation it proved to be a simple cyst

Twelve years later, at her yearly follow-up examination, I found a 1 5 cm tumor, clinically characteristic of carcinoma, at the periphery of the upper outer sector of the left breast Radical mastectomy was done 2/5/51 Study of the amputated breast showed no cystic disease The carcinoma was 3 cm in diameter and of the solid circumscribed type There were no metastases in 29 axillary lymph nodes She was well when last seen 2/23/54

We have compared the number of breast carcinomas in our series of patients with clinically evident gross cysts with the number of carcinomas that would be expected if we applied Levin's breast carcinoma incidence rates for women in New York State to the person-years of our series, by age groups Although 37 of our patients were followed for less than five years, all 200 were used in constructing a modified life table (Table 13) This table shows that the number of cases of

Table 13 Rate of Occurrence of Breast Carcinoma in a Consecutive Series of 200 Ward Patients with Cystic Disease

(Presbyterian Hospital 1930–1942)

Age	Person-years at risk	Breast cancer rate, N Y State 1945–47	Expected number of cases	Observed cases
	(2)	(3)	(2) × (3)	
20–24	4 5	0000080	00003600	
25–29	19 5	0000563	00109785	
30–34	93 75	0001742	01633125	
35–39	223 5	0003782	08452770	
40–44	449 75	0006330	28469175	1
45–49	535 0	0009629	51515150	2
50–54	441 0	0010575	46635750	1
55–59	235 5	0013039	30706845	4
60–64	112 0	0016387	18353440	
65–69	30 5	0019465	05936825	
70–74	13 5	0022977	03101895	
75–79	3 5	0026542	00928970	
Total	2162 0		1 96	8

carcinoma expected on the basis of our person-years of follow-up observation would be only about two, as against an actual occurrence of eight in our series

We fully realize that a minimal ten year follow-up period is probably too

short to provide a definitive answer to the question of the frequency of carcinoma subsequent to clinically evident gross cysts of the breast. For example, if we had been able to report a twenty year period of observation on each of our 200 patients following admission for cystic disease, more than 4 cases of breast carcinoma would be expected by applying the age specific rates for New York State The need for following patients for at least this long in a study of the relationship between the two diseases is pointed up by the fact that half our cases of carcinoma occurred more than ten years after first admission for cystic disease.

Levin has made the point that a better method of studying the problem would be through the use of a control series of women not having clinically evident cystic disease and followed for an equivalent period of time in the same clinic or hospital We have no such control series at the Presbyterian Hospital

The Frequency with Which Carcinoma is Preceded by a History of Clinically Evident Cystic Disease Another clinical method of studying the frequency of carcinoma of the breast *subsequent to* clinically evident cystic disease is to review the past history as far as the breast is concerned, of patients with carcinoma of the breast Johnson (1924) studying a series of 444 cases of carcinoma of the breast, found only 2 in which there was a history of earlier proved breast cysts. In Foote and Stewart s study of 1200 patients with breast carcinoma at the Memorial Hospital they found that only 2.4 per cent had a past history of operatively proved benign breast disease Patey reviewed the histories of 810 patients with breast carcinoma at the Middlesex Hospital and found that only 10 or 1 2 per cent, had previously had breast cysts

Presbyterian Hospital Data Regarding a History of Clinically Evident Cystic Disease Preceding Carcinoma Among a total of 1 544 patients with carcinoma of the breast coming to the Presbyterian Hospital between 1915 and 1942, only 9 or 0 6 per cent, gave a history of previous proved breast cysts The expected incidence of a history of clinically evident cystic disease in women of the carcinoma age in New York State is certainly much higher This type of evidence does not, therefore argue for a causal relationship between clinically evident cystic disease and carcinoma of the breast

The Coexistence of Cystic Disease and Carcinoma Still another kind of evidence bearing upon the relationship of cystic disease to carcinoma is the frequency with which carcinoma coexists with cystic disease One type of such evidence is provided by surgical exploration of breast lesions. It is certainly unusual to find both grossly evident cystic disease and carcinoma at exploration of a breast lesion in the great majority of cases one finds one or the other Bloodgood might be quoted as representing one extreme point of view when he stated in 1929 that in more than 500 cases in which the breast was the seat of one or more blue-domed cysts a cancer has been proved in only 5 The five cases to which Bloodgood referred were of course those in which at surgical exploration carcinoma was found to coexist with grossly evident cystic disease and both lesions were seen by the surgeon and by his pathologist in the biopsy procedure Bloodgood was not referring to the findings in laboratory studies of the entire breast made by his pathologist subsequent to radical mastectomy for

carcinoma, in the course of which gross cystic disease in addition to carcinoma was found This latter kind of evidence of the coexistence of the two diseases might be called laboratory evidence

The laboratory type of evidence of the coexistence of cystic disease and carcinoma, based upon the pathologist's careful study of the entire breast removed in the course of radical mastectomy for carcinoma, is the more accurate type of evidence, but even this evidence has limitations It is necessarily based only upon cases in which carcinoma was found and radical mastectomy performed Today, in our clinic, a very considerable proportion of patients are not treated by radical mastectomy These are, in general, the patients with the most malignant and most advanced disease We have no way of knowing whether or not the frequency of coexisting cystic disease is as great in these patients without operation as it is in those who are operated upon

Semb was perhaps the first to carry out a careful study of the coexistence of cystic disease and carcinoma in breasts removed for carcinoma He used the term fibroadenomatosis cystica to refer to the complex which we call cystic disease In a total of 122 cancerous breasts he found microscopic evidence of it in 77 per cent Grossly visible cysts (fibroadenomatosis cystica simplex) were found in 27 per cent

The most detailed study of this kind was that made by Foote and Stewart They carried out a special investigation in which cancerous and non-cancerous breasts were compared not only with regard to the presence of grossly visible cysts but also as to the frequency with which a variety of proliferative and degenerative benign lesions were found In their series of 300 cancerous breasts they found grossly visible cysts (1 mm or more in diameter) in 27 per cent

They were unwilling to estimate the frequency of microscopic cysts because they believe that an accurate estimate requires serial sectioning which they did not have Foote and Stewart preferred to study the incidence and significance of various microscopical lesions of the breast individually When they grouped together six cystic or proliferative histologic lesions which are regarded by many pathologists as components of the cystic disease complex (1, cysts, 2, duct papillomatosis, 3, blunt duct adenosis, 4, sclerosing adenosis, 5, apocrine epithelium, 6, hyperplasia of duct epithelium), one or more were present in 59 per cent of the 300 cancerous breasts which they studied

In the same year that Foote and Stewart's paper appeared, Logie presented a less detailed study of the same question from the University of Michigan He found microscopical evidence of cystic disease in 56 7 per cent of 118 breasts removed for carcinoma Kiaer, in his recent monography on the relationship of cystic disease to carcinoma, described his microscopical findings in 378 breasts removed for carcinoma He found "fibroadenomatosis" (i e cystic disease) in 60 per cent Unfortunately he fails to state how often grossly visible cysts were found

Presbyterian Hospital Data Regarding the Coexistence of Cystic Disease and Carcinoma. In the laboratory of Surgical Pathology of the College of Physicians and Surgeons the Presbyterian Hospital surgical specimens have been studied in a thorough and uniform manner for many years under Dr Stout's

direction. This material is therefore particularly suitable for the investigation of the question of the coexistence of cystic disease and carcinoma in the mastectomy surgical specimens

For our investigation of the coexistence of gross cystic disease and carcinoma we have utilized all of the mastectomy specimens studied in the laboratory between the years 1930 to 1942, inclusive There were a total of 742 breast specimens removed from a total of 713 patients, 29 of them having had bilateral mastectomy These bilateral mastectomies were usually not performed at one operative session but were done separately during the period of time (1930–1942) covered in our investigation We counted as gross cystic disease all cysts visible to the naked eye, that is, 1 or 2 mm or more in diameter This is the same criterion for the presence of gross cystic disease that Frantz used in her study of the frequency of gross cystic disease in autopsy subjects not having breast carcinoma We took care in our study not to count as cystic disease the dilated ducts of ectasia or the cystic areas of necrosis sometimes seen within carcinoma. We also utilized in searching the patient s unit history for evidence of breast cysts the surgeon s description of the pathologic lesions at operation as he saw it. We regret to say that the number of cases was very small in which the surgeon described gross cysts, although he must have seen them considerably more frequently in his biopsy procedure

The results of our study are shown in Table 14 There were a total of 713 patients with carcinoma and 176, or 24 7 per cent, of these had coexisting grossly visible cysts Twenty nine of these patients had bilateral mastectomy usually at separate operations In a few instances the contralateral breast did not contain carcinoma but was removed for other disease, or prophylactically In 17 of these 29 coexisting grossly visible cysts were found The cysts in 4 of these 17 patients were found only in the contralateral non-cancerous breast and not in the cancerous breast.

When we compare a gross cystic disease incidence of 24 7 per cent in our carcinoma series, with the 19 per cent incidence found by Frantz in her non carcinomatous autopsy series the difference is not very impressive These data are compared, from the statistical point of view in Table 15 It will be seen that the difference between the two percentages is less than twice the standard error of their difference Under conditions of simple sampling this difference could occur by chance three times in a hundred if the incidence of gross cystic disease were the same for patients in the carcinoma series and in the non-carcinomatous autopsy series. Our observed difference, therefore has no high degree of statistical significance.

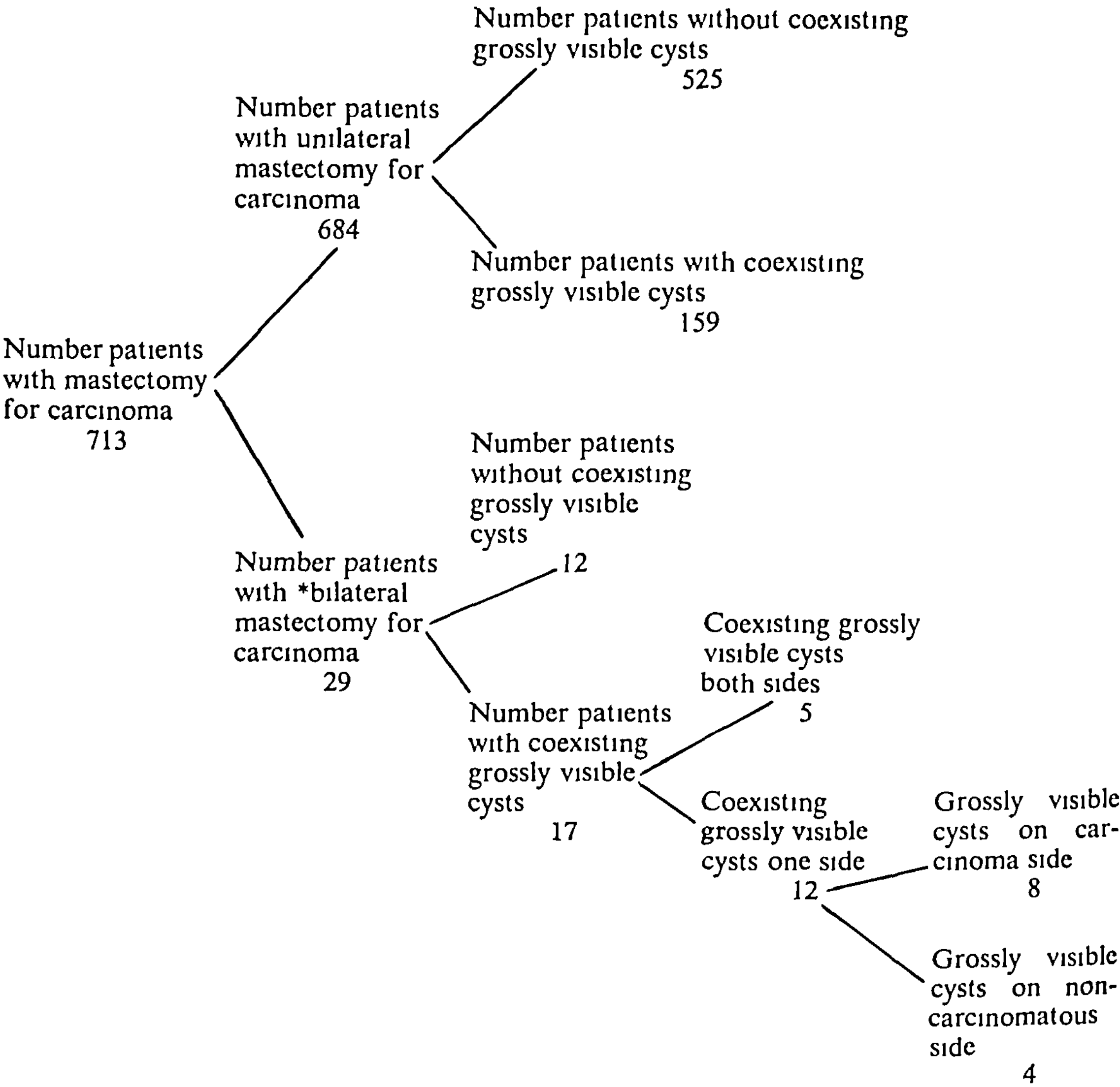
Stout has carried out a microscopical study as yet unpublished upon mastectomy specimens in his laboratory searching for microscopic evidence of cystic disease His series included 1000 mastectomy specimens removed in the Presbyterian Hospital between the years 1915–1946 His definition of cystic disease included the following lesions

1 Microscopic cysts

2. Intraductal epithelial proliferation of all benign types, including papillary proliferation

Table 14. The Coexistence of Grossly Visible Cysts and Carcinoma of the Breast in Mastectomy Specimens

(Presbyterian Hospital—Ward and Private Cases 1930–42 (inclusive))



* The contralateral breast did not contain carcinoma in 10 of these cases

3 Apocrine metaplasia of the epithelium

4 Adenosis, including both the duct type and the so-called lobular sclerosing type

Dr Stout found one or more of these features in 80 per cent of the carcinomatous breasts that he studied

To sum up, the evidence concerning the relationship of cystic disease to carcinoma must be interpreted with the basic fact in mind that the microscopic form of cystic disease exists in the great majority of the breasts of adult females in our present day population Both breasts are often involved This microscopical form of the disease is not ordinarily palpable, and therefore is not detectable clinically Gross cystic disease is found less often, perhaps in one out of every five adult women in our population Since gross cystic disease by our definition includes cysts as small as 1–2 mm in diameter, many of these patients have no palpable tumor and their disease is not detectable clinically The group of women

Table 15. The Frequency of Grossly Visible Cysts in Carcinomatous and Non-Carcinomatous Breasts

	Number of cases	Number with grossly visible cysts	Percentage with grossly visible cysts	Standard error of percentage
Patients without breast carcinoma	225	42	18 7	2 6
Patients with breast carcinoma	713	176	24 7	1 6
Difference			6 0	3 1

with gross cysts large enough to be palpable is still smaller We can only guess at the frequency of this group of patients with clinically detectable cystic disease by comparing the number of patients with cystic disease which we operate upon with the number of patients with carcinoma. On our surgical service the cystic disease patients considerably outnumber the patients with carcinoma Since at least 4 per cent of adult women in New York State today get breast carcinoma during their lifetime the frequency of clinically detectable cystic disease is certainly as great. We might hazard the guess that one out of every twenty adult women in our population has the disease at some time during her life

The evidence as to the relationship of cystic disease and carcinoma is of three types. The first consists of follow-up studies of patients with clinically evident gross cysts proved by operation These studies suggest that patients with clinically detectable and operatively proved cystic disease subsequently develop carcinoma at three or four times the expected breast carcinoma rate in the general female population It is important again to note that the carcinoma develops just as often in the opposite clinically normal breast, as it does in the breast containing clinically evident cysts. It should be emphasized that the follow up studies upon which these conclusions rest are few in number and that the follow up period is too short.

The second type of evidence concerning the relationship of cystic disease to carcinoma comes from the review of the clinical history of patients with breast carcinoma. In all of these studies the patients *give a past history of clinically* evident gross cysts proved by operation less often than we would anticipate from our knowledge of the frequency of the disease.

The third type of evidence consists of data as to the existence of grossly evident cysts, as well as the microscopic features of cystic disease in mastectomy specimens removed for carcinoma This is perhaps the most precise of the three types of evidence It *appears to show that gross cysts are not much* more frequent in carcinomatous than in non-carcinomatous breasts The frequency of microscopical cystic disease, however seems to be appreciably greater in carcinomatous breasts

Symptoms

Cystic disease of the breast *often produces no symptoms* and the patient is unaware of the disease until she discovers the tumor by palpation either acci

dental or purposeful, of the breast In other patients cysts produce pain and they may be tender to palpation These symptoms may be present continuously, or appear only in the premenstrual phase of the menstrual cycle The pain and tenderness are more apt to be present when the cyst has enlarged rapidly Perhaps they have a relationship to the tension of the fluid within the cyst Aspiration of the fluid certainly relieves them Pain and tenderness are much less apt to accompany adenofibroma or carcinoma than cystic disease

Another important clinical feature of cystic disease which helps to differentiate it from carcinoma and adenofibroma is that cysts are much more labile They develop quickly, sometimes attaining a considerable size within a few days, and they may diminish in size just as rapidly and dramatically A rapid increase in size is not infrequently correlated with the premenstrual phase of the cycle, and diminution with the postmenstrual phase When an intelligent and mentally stable patient gives a history of definite diminution in the size of her breast tumor, whether or not the diminution be correlated with the postmenstrual phase of her cycle, it is strong evidence that the lesion is a cyst and not a carcinoma

Discharge from the nipple occurs only rarely with cystic disease It is seen in intraductal papilloma and in ectasia of the ducts, two diseases that have frequently been confused with cystic disease It also occurs, but infrequently, with carcinoma

Physical Characteristics

Cysts of the breast are usually round and well delimited When they lie deep in a thick breast, near its posterior aspect, their rounded form and circumscribed character are more difficult to appreciate

Their consistency depends upon the pressure of the fluid within them When it is low they are soft, and careful palpation may sometimes detect fluctuation When they are tightly distended, however, they are firm I have the impression that their tenseness may increase in the premenstrual phase of the cycle When cysts are long-standing, and have developed thick fibrous walls, they are also firm

Cysts do not produce true retraction signs When, in a flabby breast, they attain a large size, they may, however, produce false retraction, that is, distortion of the contour of the breast adjacent to the tumor, merely as a result of its large size

Cysts are usually relatively movable in the surrounding breast tissue In this characteristic they resemble the adenofibroma, and are unlike carcinoma When, instead of a single isolated cyst, the lesion consists of a group of cysts of varied size involving a segment of the breast, the tumor which they form lacks to a degree both circumscription and movability within the breast tissue

Diagnosis

Cysts so small that they are seen only microscopically do not in my experience form a palpable tumor, and are therefore not detectable clinically

The diagnosis of cysts is in general a more serious problem than the diagnosis of fibroadenoma because the patient is apt to be older and in the cancer age

span Good circumscription and movability of the tumor suggest a cyst in these older patients. Inability to demonstrate retraction is the strongest single piece of evidence favoring a cyst

It is a great temptation to put a needle into a tumor with these characteristics and quickly and easily prove that it is a cyst I resist the temptation unless the patient has previously had a proved cyst because I believe that the knowledge of the type and extent of the cystic disease in the breast obtainable by surgical exploration and the much greater certainty of finding carcinoma by surgical exploration than by aspiration if it be present, outweigh the disadvantages of a carefully performed surgical exploration Therefore, even when the patient s tumor has the clinical characteristics of a cyst, I explain to her that the diagnosis ultimately depends upon the gross and microscopical findings, that carcinoma is unlikely but that it may be found and advise surgical exploration in the operating room, under general anesthesia with all preparations for a radical mastectomy should it be necessary

At operation when the cystic area of breast tissue has been exposed, and the tissue removed, it is always wise to ask the pathologist to section it carefully looking for areas suspicious of carcinoma and to do a frozen section Occasionally unexpected carcinoma will be brought to light by this precaution

If a patient who has previously had grossly visible breast cysts, proved by operation or aspiration comes in with a new tumor which has all the physical characteristics of a benign cyst, and none of the features of a carcinoma, I aspirate it. My procedure is to anesthetize the area with Novocain injected through a hypodermic needle and then to insert a No 19 gage needle into the tumor If I obtain the grayish or brownish fluid characteristic of a cyst, and the tumor disappears, I am content If the tumor seems solid and I get no fluid I have to fall back upon surgical exploration I try to be gentle with my aspiration efforts. In a considerable proportion of the cases in which aspiration has failed, operation will nevertheless reveal the tumor to be a cyst with a wall so dense that the aspiration needle could not penetrate it

Pathology

The gross appearance of a typical breast cyst with its dark bluish color that has given it the name blue-domed and its thin wall is well known to surgeons and pathologists When such a cyst is opened its lining is usually smooth and glistening. Large cysts sometimes have trabeculated walls (Fig 111) Occasional cysts with thick fibrous walls and a dull granular or shaggy lining are encountered They do not have a bluish color

Microscopical study shows that the lining of the larger cysts is a single layer of much flattened epithelium In many the epithelial lining has disappeared leaving a bare connective tissue surface

The fluid that cysts contain ranges from straw-colored through brown and gray to black It is usually thin enough to be drawn easily through a 19 gage needle This fluid contains formless debris Nothing is to be gained by smearing it and studying it microscopically Infrequently the cyst fluid is greenish or greenish yellow and thick and viscid

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It is unusual to find a solitary cyst. The usual gross picture is that of one large cyst surrounded by a number of small ones in the immediately adjacent mammary tissue. The entire disease process is, however in many cases grossly limited to a localized area of the breast, making it possible to excise it without too much disfigurement of the breast

Another form of localized cystic disease is that in which a limited area of the breast contains countless minute cysts, none of which is larger than 2 or 3 mm in diameter There is no larger cyst to give a rounded form and circumscription to such a lesion It gives the clinical impression of a firm not very well delimited,



Fig. 113 Both breasts cut in slices to show extensive bilateral cystic disease

but somewhat movable tumor The gross appearance of its cut surface is mottled brownish gray dotted with minute dark cysts (Fig 112) An important feature differentiating it from carcinoma is the lack of the chalk streaks that characterize carcinoma

In a smaller proportion of patients the breast is seen to be riddled throughout with innumerable cysts, many of which are large enough to form palpable tumors In this generalized form of the disease both breasts are usually involved (Fig. 113)

The microscopical features of cystic disease include the following

1 *Microcysts* We use the term microcysts for cysts so small that they are not visible grossly These appear to develop as dilatations of terminal ducts and acini (Fig 114) Cheatle thought he could trace the origin of cysts to the



Fig 111 Large trabeculated cyst of breast.





Fig 112 Many small cysts forming a tumor of the breast

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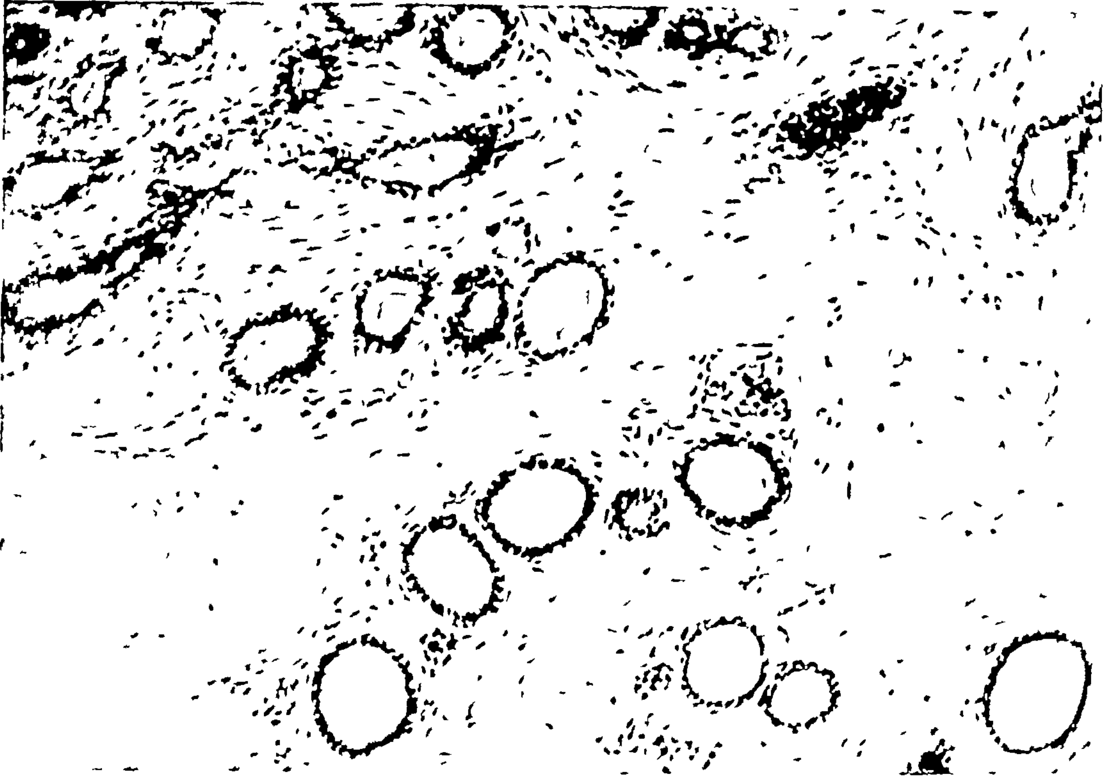


Fig 114 Microcysts of the breast

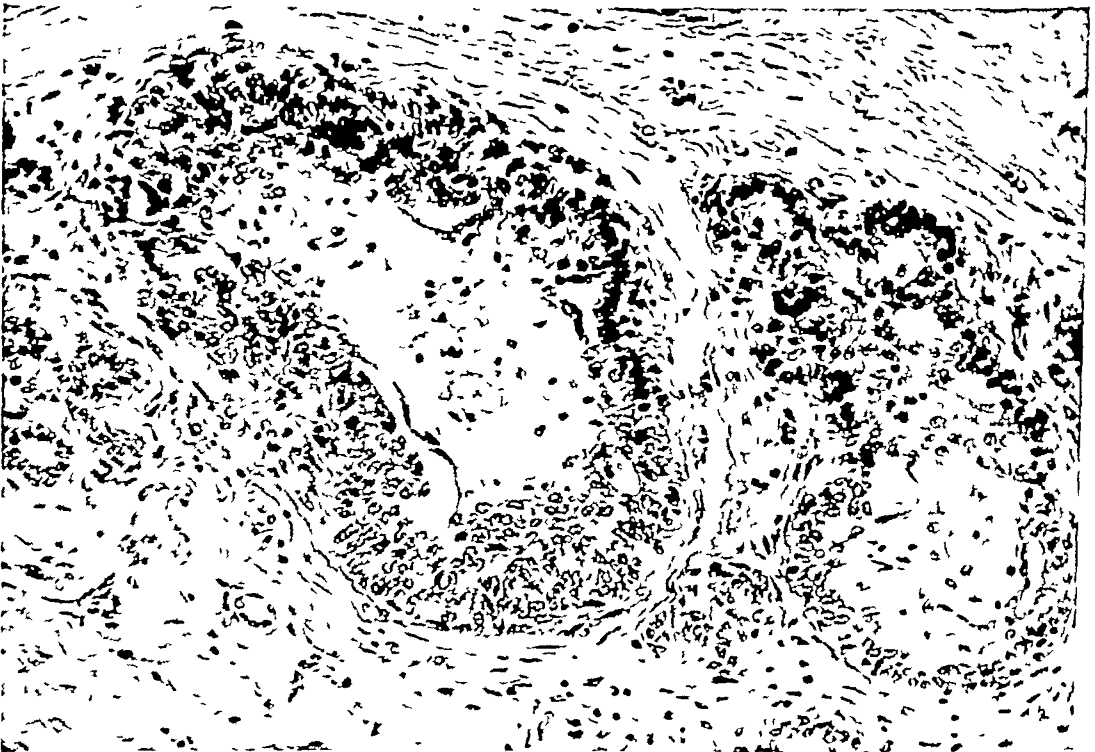


Fig 115 Heaping up of the duct epithelium in cystic disease

acini exclusively The cysts are not infrequently so numerous that it seems impossible that they could have originated from the larger ducts alone, since there could not have been enough of these to form the multitude of cysts The process by which the cysts develop is obscure—certainly there is no evidence that obstruc-

tion of the ducts is responsible The epithelial proliferation which is almost always a feature of cystic disease makes one believe that the process is a hyper plastic and not an atrophic one

2 *Proliferation of the Epithelium* The epithelium lining the small cysts and dilated ducts shows a great variety of types of proliferation The simplest form is a simple heaping up of duct epithelium (Fig 115) In its extreme form this proliferation may be many layers thick and largely fill the lumen of the dilated duct (Fig 116) Follow up experience has taught us in Stout s laboratory that even the most extensive proliferation of this kind implies no increased threat of carcinoma provided that the individual proliferating epithelial cells maintain benign characteristics There are, of course, several types of intraductal

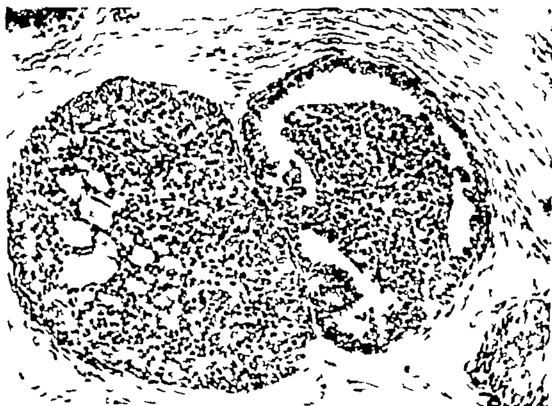


Fig 116 Epithelial proliferation filling ducts in cystic disease

carcinoma in which the ducts are filled with cells The pathologist must learn to recognize their special pattern and to distinguish them from the benign proliferation accompanying cystic disease. I will describe these intraductal forms of carcinoma in Chapter 21

The proliferating epithelium in the small cysts and dilated ducts often has a papillary pattern This may consist merely of low irregular projections of the duct epithelium into the duct lumen These papillae coalesce to form a lace like pattern filling the duct lumen Fully developed branching papillae with thick stalks (Fig 117) are often seen The process usually involves a number of ducts or groups of ducts and is intermingled with the other microscopic lesions of cystic disease (Fig 118)

These microscopic papillomas, widely dispersed throughout the dilated ducts and small cysts of cystic disease should be distinguished from a macroscopic

Fig 117 Intraductal papillary proliferation in cystic disease.

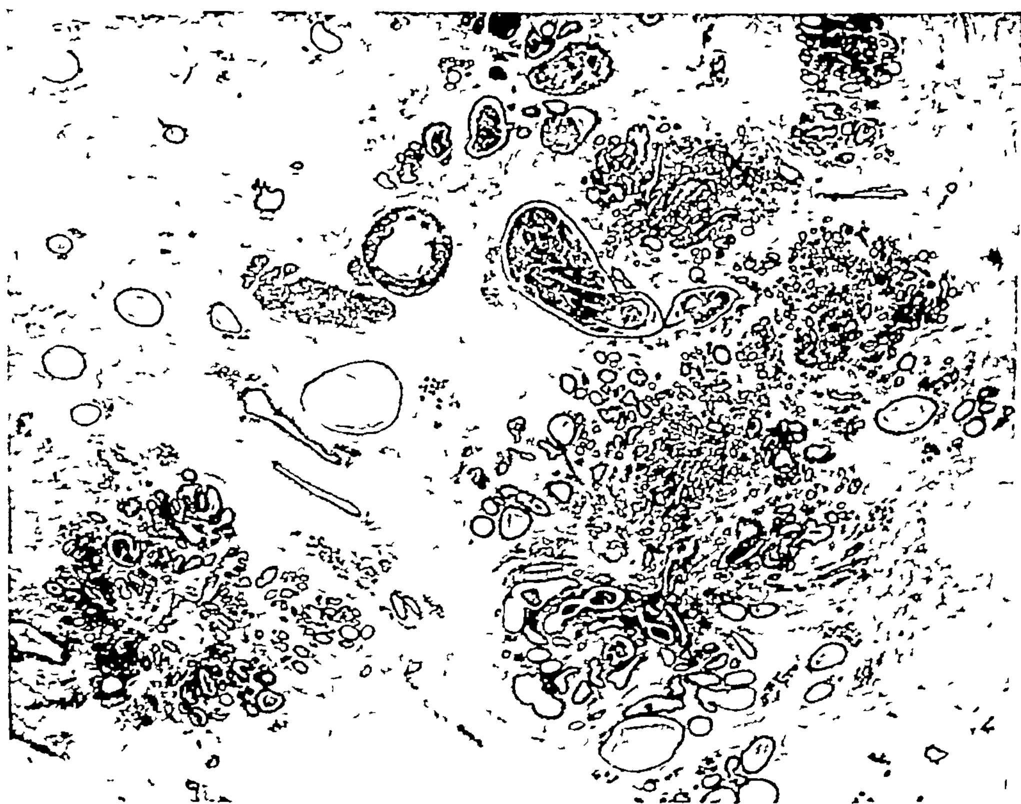


Fig 118 Variegated epithelial proliferation in cystic disease

papilloma, arising from the wall of a single main duct, usually in the subareolar region near its termination The latter lesion constitutes a separate clinical disease, which I will discuss in Chapter 13

3 *Metaplasia of the Epithelium* Apocrine metaplasia of the duct epithelium is another feature of cystic disease. The normal low cuboidal cells are transformed into the so-called apocrine" or "pale type—cylindrical in shape, with small rounded nuclei and a relatively prominent, pale acidophilic cytoplasm (Fig 119) This transformation may involve only a small sector of the lining epithelium of a single duct or the entire lining of a number of ducts and small cysts may be affected



Fig. 119 Papillary proliferation of the apocrine type of epithelium in cystic disease

The significance of this apocrine epithelium remains unknown. In the rhesus monkey Speert produced apocrine metaplasia of the breast epithelium by the administration of very large doses of estrogen This form of epithelial metaplasia does not seem to have any relationship to carcinoma in either man or animals

4 *Adenosis* Adenosis is a term popularized by Ewing to describe the benign multiplication of ducts and acini which is one of the microscopical features of the cystic disease complex. It is usually a minor component of the complex and is intermingled with intraductal epithelial proliferation of various types and with cysts of all sizes, as seen in Figure 118 Adenosis does not have much importance therefore, as a component of cystic disease When adenosis dominates the path

ological picture and forms a solid tumor without gross cysts, however, it becomes a lesion of great practical importance because its infiltrative character leads pathologists to mistake it for carcinoma Chapter 8 is devoted to this tumor-forming type of adenosis, and since I include a detailed description of the microscopical character of adenosis in that chapter, I have not included such a description here in discussing adenosis as it forms a minor component of the cystic disease complex

The Pathological Classification of Cystic Disease

I believe that it is important for pathologists to specify in their diagnoses of cystic disease whether they refer to the finding of grossly visible cysts, or only to the microscopical features of cystic disease The diagnosis should read "cystic disease—gross" and "cystic disease—microscopical," or only "cystic disease—microscopical "

This distinction has an important disciplinary value for the surgeon, who must, through correlation of his clinical findings with the pathologist's studies, learn to distinguish clinically recognizable disease in the breast from increased nodularity representing only physiological variation in the breast This distinction is the fundamental one which a physician must learn to make correctly if he is to avoid missing disease on the one hand, or advising operation unnecessarily on the other hand The latter error is, I believe, the more frequent one, at least among surgeons

Grossly visible cysts in the breast often form a tumor which is palpable and therefore clinically recognizable The breast lesions consisting solely of the microscopical features of cystic disease, without any grossly visible cysts, usually do not form a tumor and cannot be detected by clinical examination When a surgeon biopsies a breast tumor and finds grossly visible cysts, his operation is justified But when he biopsies what he regards as breast disease and finds only the microscopical features of the cystic disease complex, and no other breast disease, his biopsy is usually not justified He should not have operated What he thought to be a tumor was only increased nodularity within the limits of physiological variation True enough, microscopic cystic disease is found, but it exists in the majority of all clinically normal breasts and, being undetectable, cannot be regarded as an indication for operation If the pathologist does not distinguish between gross cystic disease and microscopic cystic disease in his report, the surgeon has no way of recognizing his error When he gets the usual report of "chronic cystic mastitis" he will assume that his operation was justified, when in fact it may not have been

Clinical Course

We have mentioned, in our discussion of the symptomatology of cystic disease that cysts may increase or decrease in size more quickly than other breast tumors It is not unusual for a cyst to disappear entirely over a period of a week or two This fact made me adopt the rule of always reexamining my patient after admission to the hospital on the afternoon before operation Unless a surgeon takes this precaution, he will one day be chagrined to find in the operating room that the tumor that was indubitably present when he last examined his patient some

days previously is no longer palpable. It is pleasant to discover this fact before operation but deplorable to learn it in the operating room

After the first cyst or cysts have been excised new cysts subsequently appear in a considerable proportion of patients In our series of 147 patients followed for ten years or more, one third developed further cysts as shown in Table 16

Table 16. New Grossly Visible Cysts in 147 Patients Followed 10 or More Years

	Number	Per cent
In same breast only	17	11 6
In opposite breast only	15	10 2
In both breasts	15	10 2
Total	47	32 0

Rate of recurrence which involved opposite breast 30 47 or 63 8 per cent of all patients with recurrences.

As indicated in this table in about two-thirds of the patients, recurrent cysts were in the breast opposite to that in which the original cyst was found This experience confirms the bilateral nature of cystic disease

The interval between the detection of the first cyst and successive appearance of clinically evident cysts may be a long one, as indicated in Table 17 In 5 of our 47 patients who developed clinically evident recurrent cysts the interval was 10 years or more

Table 17 Interval Between Original Diagnosis of Breast Cyst and the First Subsequent Cyst in 47 Patients Followed 10 Years or More

Years after original diagnosis	Number of patients
1	5
2	6
3	5
4	6
5	5
6	8
7	3
8	3
9	1
10 or over	5
Total	47

Therapy

I have emphasized in discussing the diagnosis of cystic disease that surgical exploration is the right procedure for proving that a breast tumor is indeed a cyst, and for ruling out carcinoma in patients in whom the diagnosis has not been previously established pathologically

The incision for exploration should be made as I have described in discussing the technique of excision of benign tumors in Chapter 6 It should be placed in the skin lines and somewhat medial to the tumor if the lesion lies near the periphery

of the breast If the tumor is more centrally situated it can usually be exposed through a circumareolar incision. A radial incision should never be made

When the cyst has been exposed, it is my practice to open it so that its content and inner surface can be inspected This precaution guards against the mistake of locally excising a cystic papillary carcinoma Emptying the cyst has another advantage Its collapsed wall, together with surrounding diseased mammary tissue, can be more easily excised and delivered through a limited incision than can the intact cyst Whatever the surgeon can do to minimize the size of the incision and the extent of the surgical trauma in operating for a benign lesion like cystic disease is certainly worth while It is perfectly permissible to excise only part of the wall of a cyst if complete excision will unreasonably deform the breast Such a partial excision is just as efficacious in doing away with a simple cyst as complete excision

In excising the collapsed cyst I try to maintain as good hemostasis as possible, carefully clamping small vessels as I cut them and keeping the wound from filling with blood Blunt dissection, as with scissors, is impossible in the breast and should never be attempted the excision should be done with the scalpel It is essential to keep the wound reasonably dry because the surgeon must be able to see the extent to which the cystic disease involves the breast tissue surrounding the main cyst, and to see carcinoma should he encounter it adjacent to the cystic disease

When a great part of the breast is found to be involved by the cystic process, so much so that complete excision will badly deform the breast, I do not attempt it I know that it is impossible, in these patients with extensive cystic disease, to excise all of the lesion without performing bilateral mastectomy, a procedure which I believe unjustified except under certain special circumstances

When the local excision of the diseased area of the breast has been completed, the bed of the wound should be carefully inspected and palpated to make certain that the tumor has indeed been found and removed Palpation is best done with the flat of the fingers over the area, as in clinical examination The surgeon will occasionally be surprised to find that yet another tumor remains in the nearby breast tissue

When a new tumor having the clinical characteristics of a cyst develops in one of my patients in whom the presence of gross cysts has previously been proved by surgical exploration, I aspirate it If I obtain the characteristic cyst fluid, and the tumor disappears, nothing more need be done It is surprising, yet true, that aspiration of the fluid from a simple blue-domed cyst almost always does away with it It is rare that fluid reaccumulates in the same cyst and requires further aspiration It seems unlikely that the cyst continues to be collapsed because newly accumulating fluid leaks out through the needle hole in its wall It is more reasonable to suppose that decompression in some way interrupts the mechanism by which fluid accumulates within cysts

With this plan of therapy I avoid repeated, and I believe unnecessary, operations upon patients with cystic disease I believe that the risk of missing a carcinoma by aspiration used in this limited manner is negligible

Warren's recommendation that mastectomy be performed when further cysts develop seems to me unjustifiably radical This must of course be bilateral

mastectomy although Warren did not recognize this implication for cystic disease is usually bilateral, and recurrent cysts, and carcinoma, if it develops, appear just as often in the opposite breast as in the one in which the first cyst occurred. The question that we must ask ourselves, therefore is How great must the danger of carcinoma be in women with proved gross cysts to justify prophylactic bilateral mastectomy?

Every physician who serves his patients with understanding and compassion knows that bilateral mastectomy is a heavy penalty for the normal woman I doubt that physicians whose lives are passed in the laboratory and who have not had direct and continuing responsibility for patient care fully understand the problem.

I have presented data that suggest that in women with clinically evident, proved gross breast cysts the incidence of subsequent carcinoma is greater than in women in the general population Yet the available evidence as a whole bearing upon the relationship of gross cysts to carcinoma is not entirely consistent I do not believe that the threat of carcinoma justifies prophylactic bilateral mastectomy This is of course, only a personal opinion but I believe that most women will agree with me.

There is an alternative method of protecting women with proved gross breast cysts against carcinoma. It is frequent clinical examination of the breast. If the patient can be taught to palpate her own breasts expertly she has the protection that monthly examination provides If she is not stable enough to do this, her breasts should be examined by a physician at least every three months for the rest of her life. This is frequent enough so that a carcinoma, should it develop may be detected while it is yet in a curable stage. The breasts, in these women who are being followed should be kept free of tumors by aspiration of the new cysts that develop so that a carcinoma will not be missed because it is hidden among other tumors

In patients in whom both breasts are riddled with cysts—cysts so numerous that it is impractical to attempt to get rid of them by aspiration—the difficulty of detecting a carcinoma developing among them becomes much greater These are the only patients in whom I have seriously considered prophylactic bilateral mastectomy Fortunately patients with such extensive cystic disease are few When they get past the menopause their disease begins to regress I confess that I have invariably temporized with them and have not personally performed bilateral mastectomy on anyone for cystic disease.

There has been a good deal of indiscriminate hormonal therapy for cystic disease Both androgens and estrogens have been used Since we do not know the nature of the underlying hormonal imbalance in cystic disease if indeed there be any hormonal therapy is necessarily empirical and may well do harm instead of good I have seen in consultation a good many patients with cystic disease who had been given one or another hormone and I have not been able to find any evidence of benefit Some women given androgen have developed the unpleasant side effects that androgen regularly produces when it is given in sufficient doses Other patients given estrogen for cystic disease a form of therapy enthusiastically recommended by Lewis and Geschickter a few years ago have seemed to have their breast condition aggravated This is what we should expect

of course, if cystic disease is at least in part due to estrogen, as the experimental evidence in fact suggests

Irradiation has sometimes been used for cystic disease It is entirely ineffective and I only mention its use to condemn it

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CHAPTER 8

ADENOSIS

In describing, in the preceding chapter the microscopical features of the com plex lesion that we call cystic disease I have already referred to the component that we call for lack of a better name, adenosis The acini of the gland fields and to a lesser extent the small ducts proliferate invade the breast stroma and finally stimulate fibrosis which has led to the name of sclerosing adenosis As a common and relatively inconspicuous feature of cystic disease adenosis gives no trouble to the clinician When adenosis dominates the microscopical picture however and produces in itself a dominant tumor of the breast, the pathologist is more likely to mistake it for carcinoma than almost any other lesion that de velops in the mammary gland. For this reason I wish to devote this chapter solely to the form of adenosis that produces a tumor The reader should not assume that I regard this tumor forming kind of adenosis as being necessarily any different in its essential nature from the adenosis of ordinary cystic disease Yet this tumor forming adenosis deserves separate consideration because it has clinical characteristics and presents a special diagnostic problem of great im portance

Incidence

In defining this tumor forming type of adenosis pathologically I refer to the lesions in which the tumor is actually formed by the adenosis No gross cysts, excepting in some instances a few minute ones measuring not more than one or two millimeters in diameter are seen

Adenosis of this type forming a tumor has been relatively infrequent in our Presbyterian Hospital experience I must admit that some pathologists and a good many surgeons are not familiar with this lesion and it is often missed, being lost in the hodge podge of conditions that are lumped together under the ambig uous term cystic mastitis I have collected 35 cases of adenosis tumor mostly in my own patients, operated upon between the years 1939 and 1955 I would estimate that one might encounter one case of adenosis tumor to every 25 or 30 cases of carcinoma Heller and Fleming described a series of 15 cases of adenosis tumor and stated that this lesion constituted 2 per cent of all breast lesions in their clinic

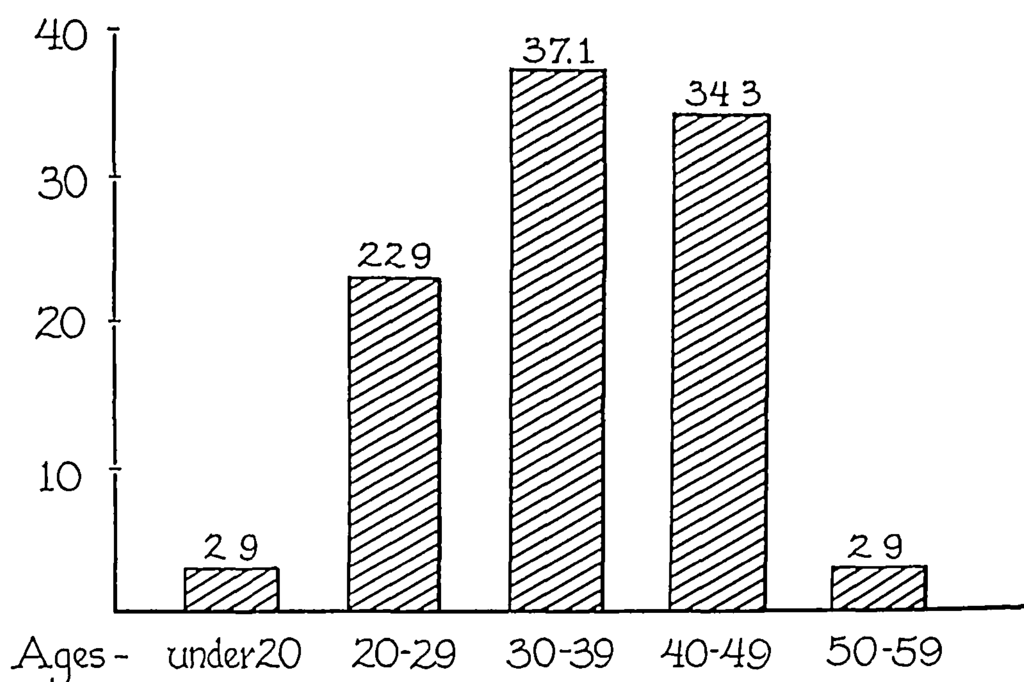
The average *age* of our group of patients with adenosis tumor was 35 years The youngest was 19 The oldest was 52 It is therefore fair to say that this disease evolves during the menstrual phase of life and is most frequent in the middle years of menstruation (Chart 2)

Etiology

Seven of our 35 patients were single women Among the married women 5 had never been pregnant, 19 others had produced 43 living children, and in the remaining four the information as to parity was lacking These data do not suggest that the patients with adenosis tumor had anything abnormal in their reproductive history.

Clinical Features

Adenosis produces a tumor which may be clinically indistinguishable from carcinoma It is firm and poorly delimited in the area of breast tissue in which it



Percentage distribution of ages in 35 patients with adenosis

Chart 2

lies It is also somewhat fixed in the breast tissue, like a carcinoma Adenosis does not ordinarily produce retraction signs, although in a few cases where the lesion lay superficially in the breast, I have seen minimal retraction in the overlying skin But this absence of retraction does not assist the clinician very much in his effort to distinguish between adenosis and carcinoma, because most of the tumors produced by adenosis are comparatively small, and the clinician should know that small carcinomas sometimes produce very little, if any, retraction

Tumors produced by adenosis are in general small The average diameter of the tumor in the 35 cases in my series was only 2 6 cm The tumors varied individually from 0 8 to 5 cm In the case of this one large 5 cm tumor, which is unique in my experience, a great part of the upper outer sector of the breast was replaced by confluent nodules of adenosis The average diameter of a tumor due

to adenosis has been less than half that of the average carcinoma coming to our clinic.

The clinical characteristics of adenosis do not, therefore distinguish it in any way from carcinoma As a result these tumors due to adenosis are often diag nosed clinically as carcinoma and the surgeon comes to the operating table with this suspicion in his mind

Pathology

There are certain gross features of typical adenosis that should suggest to the critical pathologist that he is dealing with adenosis and not with carcinoma Although adenosis is firm in consistence it is not apt to be as hard as most carcinomas The cut surface is slightly brownish owing to the presence of small granular brownish areas, which are in fact the foci of proliferating acini (Fig

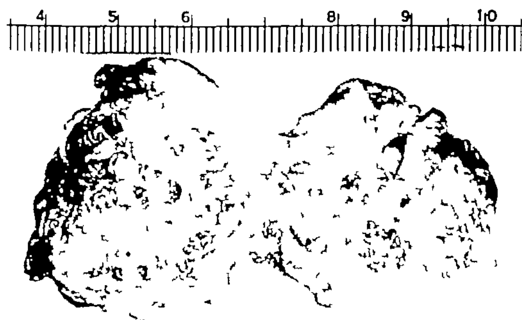


Fig 120 The gross appearance of a tumor formed by adenosis.

120) The grayish white streaks so typical of carcinoma are not usually seent None of these gross features are, however sufficiently characteristic to permi even the most experienced pathologist to distinguish surely between adenosis and carcinoma.

The microscopical features of adenosis also may superficially resemble car cinoma. Adenosis is of two histological types—in one the small ducts multiply and in the other the growth stimulus affects chiefly the acini and often has a lobular pattern

The ductal type of adenosis gives the picture of scattered groups of small ducts, which seem to represent a budding of the duct system without the forma tion of terminal lobules of acini (Fig 121) Stewart believes that these newly formed ducts end blindly and he therefore calls this form of adenosis "blunt duct adenosis However they may originate these newly formed small ducts are often a feature of the microscopic pattern of cystic disease They are some

Fig 121 Ductal type of adenosis

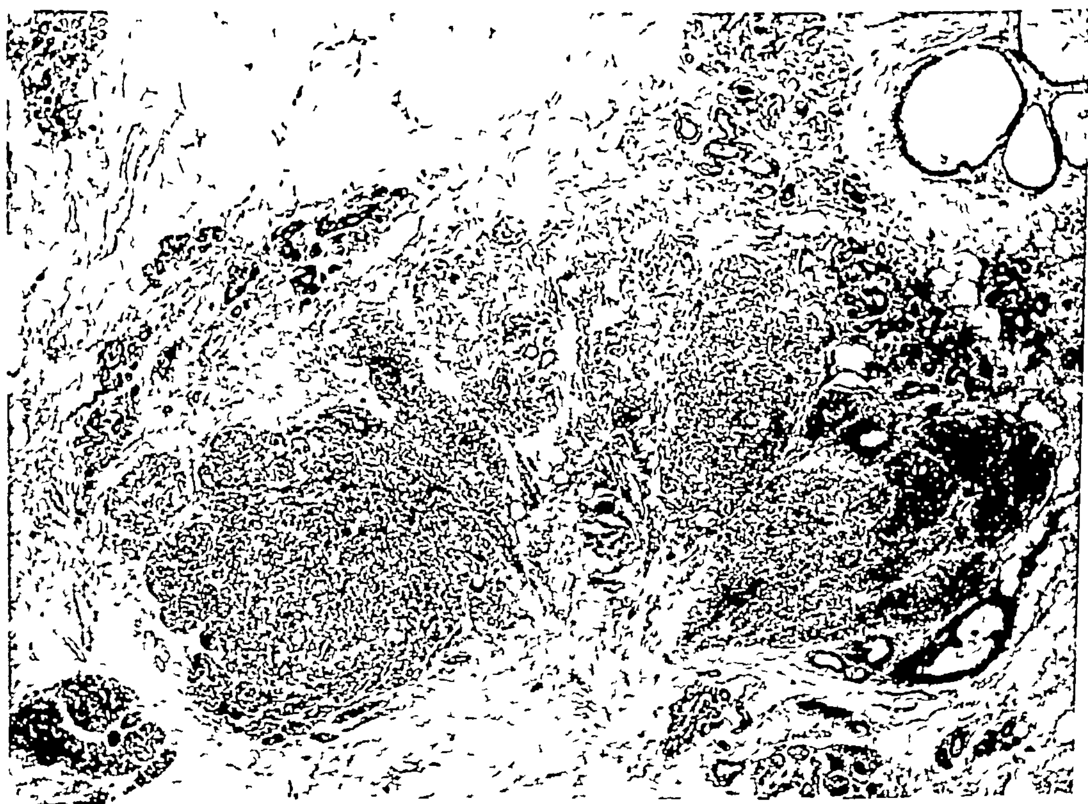


Fig 122 Acinar type of adenosis

times grouped into patterns vaguely reminiscent of incomplete lobules, but more often they have no orderly arrangement, and are scattered irregularly throughout the diseased area of the breast The individual newly formed ducts vary a good deal in size, and it is tempting to assume that the larger ones evolve into cysts

The acinar type of adenosis in which the acini appear to multiply in a lobular pattern is the more frequent type of adenosis Because this form of adenosis in its mature stage is characterized by fibrosis it has been called sclerosing adenosis " In the early or florid, stage of this process, the acini multiply and the lobules increase in size They push out into the surrounding breast stroma, but still retain a lobular pattern as may be seen in Figure 122 The epithelial proliferation is so *vigorous that the lumens of the acini are filled up and their outlines are almost* entirely lost, as a higher power view (Fig. 123) of the same lesion shows In this early stage of the process no considerable degree of fibrosis has developed to distort the appearance of the lesion The individual proliferating cells (Fig 124) although smaller than most breast carcinoma cells and varying less in size and shape, occasionally show mitosis and have enough variability to make it difficult to be certain from their character alone, that the lesion is not a carcinoma.

As the lesion ages fibrosis develops The lobular pattern is somewhat obscured, and the individual proliferating cells are compressed and distorted so that they appear to stream out into and infiltrate, the breast stroma, as seen in Figure 125 The individual proliferating cells at this stage appear rather smaller with denser *more compact nuclei which usually do not show mitosis (Fig 126) They lie in a* fibrous matrix that separates the cells from one another and encircles the acini which can still be identified

At a yet more advanced stage of fibrosis, adenosis may give a picture in which the effects of the fibrosis have so distorted the morphology of the original lobular proliferation that it can scarcely be recognized as such Figure 127 is an example of this extreme degree of fibrosis Such a microscopic field is strongly suggestive of carcinoma

When the pathologist already suspicious that he is dealing with carcinoma because of the clinical character of the lesion and its gross appearance studies his frozen section and sees small epithelial cells indubitably infiltrating the breast stroma he is very apt to mistake adenosis for carcinoma. He can save himself from the mistake only by always keeping adenosis in mind when he studies frozen sections of breast lesions and by deferring his definitive diagnosis if he has the *slightest doubt about the nature of the lesion He must cultivate a state* of mind in which he takes no chances at all with this differential diagnosis He must never gamble If he will only wait, and prepare and study with sufficient care, *an adequate number of paraffin sections* he can distinguish correctly between adenosis and carcinoma every time

The surgeon on his part, when told that a reliable frozen section diagnosis is not possible, must not complain of his pathologist s uncertainty Rather he should be grateful that he has a pathologist who puts accuracy above everything else He should close the wound after locally excising the small tumor from which *he has* excised the biopsy for the frozen section and wait until the definitive diagnosis is available If the surgeon proceeds with radical mastectomy when his pathologist is doubtful of the diagnosis he runs a risk of doing a needless mutilat

Fig 123 Acinar type of adenosis in its florid stage—higher power

Fig 124 The individual proliferating cells of the acinar type of adenosis in its florid stage

Fig 125 Acinar adenosis in its sclerosing stage.

Fig 126 The individual cells of acinar adenosis in its sclerosing stage

ing operation This is a far greater threat to the patient than waiting a few days for the paraffin sections that make possible a sure diagnosis, should the tumor prove eventually to be a carcinoma We have no proof at all that a week's delay under these circumstances prejudices the patient's chance of cure

The pathologist trying to distinguish adenosis from carcinoma, either in frozen or in paraffin sections, will find that his best reliance is not the high power cytology of the lesion, but its low power histology The patchy distribution of the foci of proliferating cells, suggesting a lobular origin, is the best indication that the lesion is adenosis Figure 128 illustrates this feature The following two cases of adenosis illustrate the diagnostic difficulties that these lesions present

Case 1 Mrs M O, a housewife aged 47, had discovered while bathing a small tumor in the upper outer sector of her left breast a year before she consulted me She

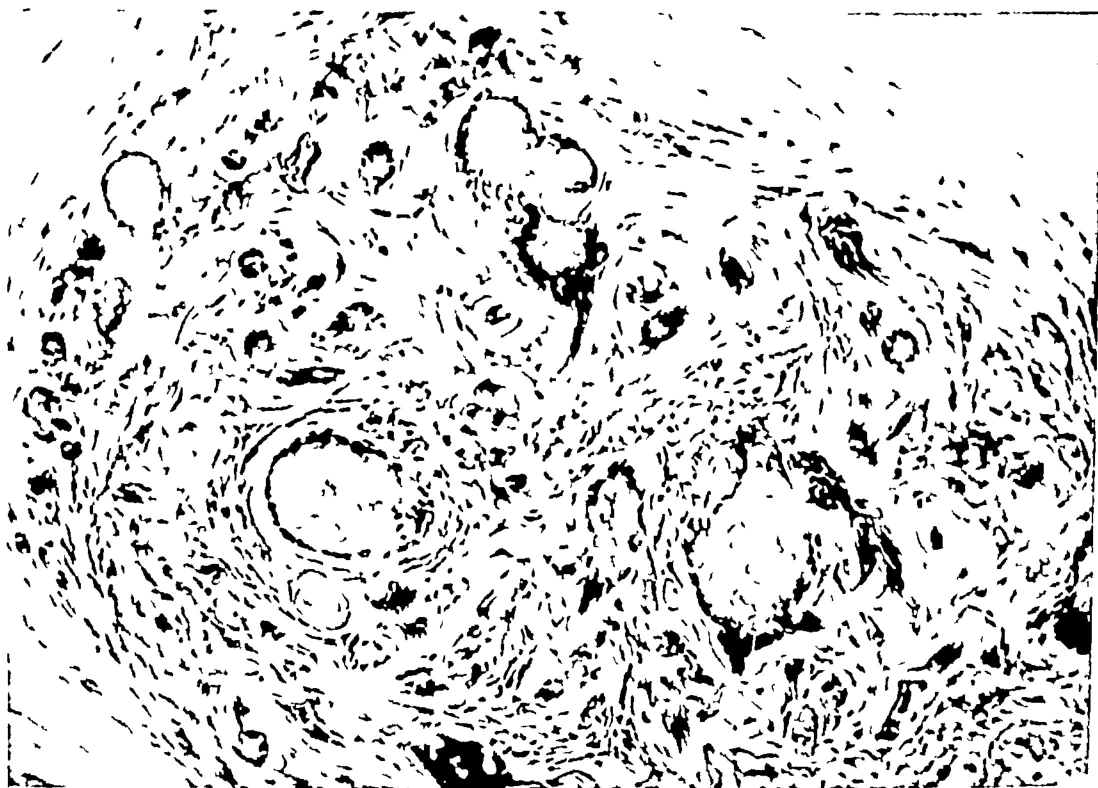


Fig 127 Adenosis with an extreme degree of fibrosis, simulating carcinoma

disregarded it because it almost disappeared after each menstrual period Recently it had grown in size

Examination showed a 3 cm tumor situated in the radius of 2 o'clock, 3 cm beyond the edge of the areola of the left breast It was firm, not very well delimited from the surrounding breast tissue, but fairly movable in it There was no retraction and there were no enlarged axillary nodes

With all preparations made for a radical mastectomy should it prove necessary, a short incision was made over the lesion and a small wedge excised for frozen section The cut surface was firm and grayish-white, and suggested carcinoma The frozen section was tentatively diagnosed by the pathologist as well differentiated carcinoma I demurred because the lesion seemed more like adenosis to me After studying several frozen sections we agreed to wait for paraffin sections I excised the remainder of the tumor and closed the wound The paraffin sections that were ready twenty-four hours later showed only adenosis with marked fibrosis

This case illustrates how great the difficulty may be in interpreting frozen sections of adenosis and the wisdom of deferring radical surgery if there is even a shadow of a doubt about the nature of the lesion

Case 2 Mrs E. B., aged 45 consulted me because of a discharge from her right nipple. It had first appeared six months previously when she noted a serous discharge over a three day period She went to her family doctor who found no tumor in the breast and dismissed her There was no further discharge for five months, when she noted a few drops of bloody discharge on her brassiere

Palpation revealed only a poorly defined area of induration between the radii of 11 and 1 o clock, just beyond the edge of the areola of the right breast It was not well enough delimited to measure accurately It was relatively fixed in the breast tissue. There was no retraction Pressure over the induration produced a drop of serum from a nipple duct situated in the radius of 11 o clock



Fig 128 Low power view of adenosis illustrating its patchy distribution

With all preparations for a radical mastectomy should it prove necessary the area of induration was exposed through a circumareolar incision. It was seen to be due to the presence of a great many firm brownish nodules scattered throughout the softer whitish breast tissue These nodules varied from a few millimeters to a centimeter or more in diameter The entire upper outer sector of the breast was involved by the process. Several of the nodules were excised for frozen section which revealed characteristic adenosis To remove all of the lesion would have meant sacrificing almost one half of the breast This seemed unjustified. Only the most prominent part of the lesion that which had produced the area of induration was excised A year has since gone by without any evidence that the disease left behind is growing.

Treatment

Adenosis requires only local excision Mastectomy is certainly not justified.

Carcinoma has not developed subsequently in a single one of our patients treated by local excision

The importance of adenosis tumor lies, indeed, entirely in the danger that it may be mistaken for carcinoma and unnecessary mutilating surgery performed

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CHAPTER 9

FIBROUS DISEASE OF THE BREAST

The breast lesion that we call fibrous disease is not generally recognized as a disease entity It is a benign localized but not encapsulated, proliferation of the breast stroma that forms a definite dominant tumor Because it is one of the less frequent benign lesions of the breast, its identity has usually been lost among the heterogeneous group of breast lesions that incurious pathologists and surgeons lump together as 'fibrocystic disease Unless pathologist and surgeon really try to help each other identify fibrous disease, neither will succeed in doing so This lesion is worth while searching out and identifying, however because it has characteristics that are important clinically

Age Distribution

Fibrous disease develops during the second, third and fourth decades, and is rarely seen after the menopause It has, therefore, much the same age incidence as cystic disease In a series of 38 personal cases that I dealt with from 1948 to 1953 the median age was 39 5 years The youngest patient was 23 and the oldest 54 The age distribution of these patients is shown in Chart 3

Racial Predilection

In my series of cases of fibrous disease there is no indication of any special racial predilection for the lesion

Multiplicity

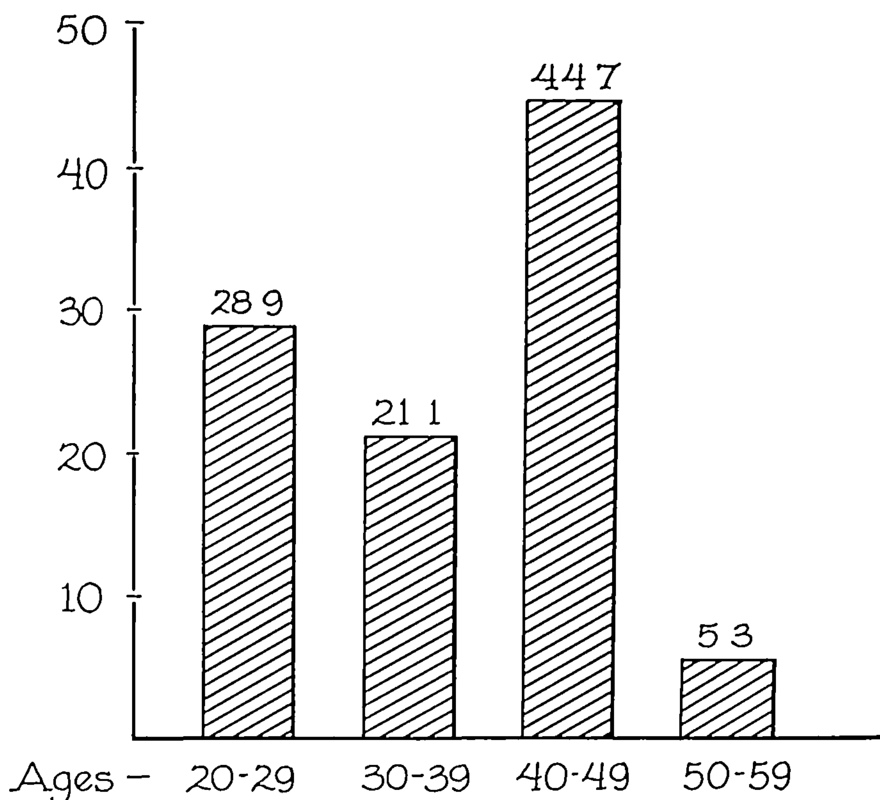
Fibrous disease has a tendency to be bilateral and to be symmetrically situated in the upper portion of the outer half of each breast In 5 of my 38 cases there were such bilateral symmetrical lesions In one other patient there were two separate areas of fibrous disease in the upper half of one breast.

Etiology

The development of fibrous disease during the period of greatest ovarian activity suggests of course that it is caused by some form of hormonal dysfunction This disease is the best example of selective stimulation of the fibroblastic element of the breast structure because there is no associated epithelial proliferation

There is good clinical evidence that the patients in whom fibrous disease of the breast develops are women with some sort of hormonal dysfunction They are

apt to be women with abnormally large pendulous breasts They often have hair in the areolar region, and a suggestively male configuration of the pubic hair They are apt to be sterile In my series of 38 patients with fibrous disease of the breast 7 were unmarried Of the 31 who were married, 15 had never been pregnant The 16 who had become pregnant had produced a total of only 22 children Five of these children had been delivered by cesarean section This is certainly an abnormally low fertility record



Percentage distribution of ages in 38 patients with fibrous disease

Chart 3

Symptoms

Fibrous disease makes itself evident by the formation of a painless tumor There are no other symptoms Occasional patients will complain of some degree of pain and tenderness in the region of the tumor, but careful inquiry will usually bring out the fact that these sensory phenomena developed after the patient discovered her breast tumor, and were probably suggested by its presence

Physical Characteristics

The tumor of fibrous disease is not well delimited like a cyst or an adenofibroma Its edges merge into the surrounding breast tissue This single characteristic is enough to alert a skilled examiner to the possibility of carcinoma

Its shape is usually irregularly discoid It is not round like a cyst or an adenofibroma

It is firm in consistency but not hard like a carcinoma This is perhaps too fine a distinction to hope to make, particularly when the tumor is situated in a large dense, comparatively nodular breast.

The fibrous disease tumor lacks the easy movability of a cyst or an adenofibroma. It does not seem to slide around beneath the examiner s fingers It is somewhat fixed in the bed of breast tissue in which it lies This fixation is not as marked however as with carcinoma Again this may be too finely drawn a distinction

An important differentiating feature between fibrous disease and carcinoma is that fibrous disease does not produce retraction while some manifestation of retraction can be demonstrated in almost every carcinoma

The fibrous disease tumor does not attain a large size The majority are from 2 to 3 cm in diameter In my series of 38 recent cases none of the tumors were larger than 5 cm in diameter The difficulty of differentiating the various tumors of the breast from one another is greater the smaller they are and the small size of the fibrous disease tumor often adds to the difficulty of identifying it clinically

These tumors have a great tendency to be situated in the outer upper portion of the breast. This is of course the most frequent site for most breast tumors but in fibrous disease the predilection for this sector is greater than for other tumors In 30 of my series of 38 recent patients with fibrous disease the lesion was in the middle or upper portion of the outer half of the breast

Diagnosis

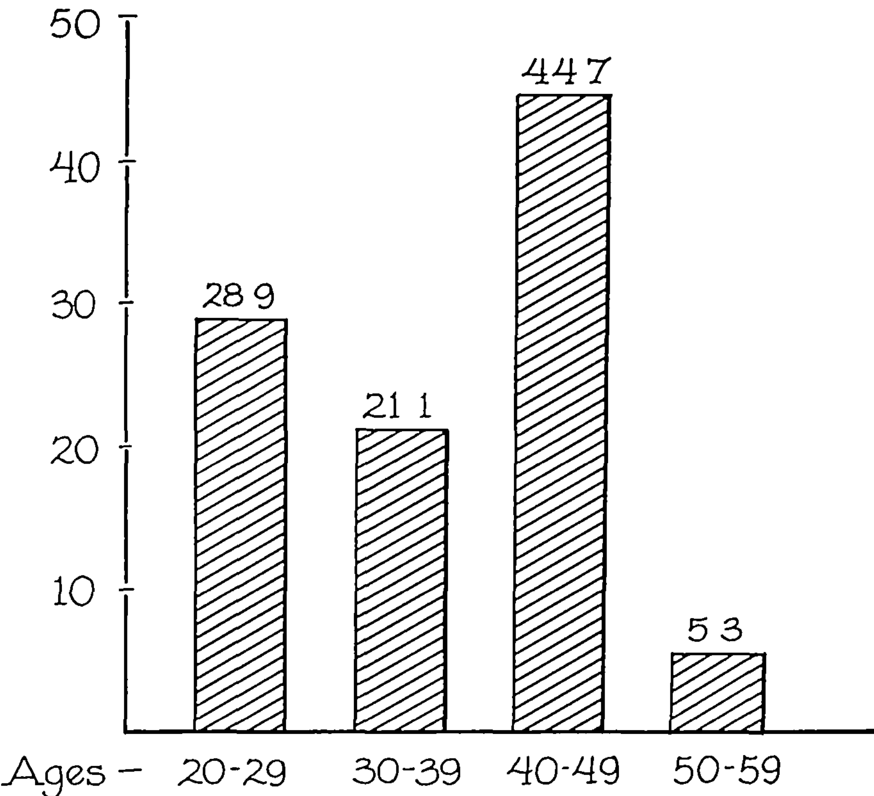
The fibrous disease tumor resembles carcinoma more than it does an adenofibroma or a cyst In the majority of cases clinical examination leaves the examiner in doubt as to the true nature of the lesion If the patient is postmenopausal she probably does not have fibrous disease

Pathology

The fibrous disease tumor is not encapsulated and merges into the surrounding breast tissue Its cut surface is abnormally firm with a dense tough texture (Fig 129) The knife does not grate going through however as it often does with carcinoma. Fibrous disease is more whitish in color and more uniform in appearance than normal breast tissue It lacks the ominous chalky streaks of carcinoma. While the pathologist cannot be entirely certain that he is dealing with fibrous disease from its gross characteristics he should strongly suspect the correct diagnosis

When it comes to recognition of fibrous disease from its microscopical features, however the pathologist faces greater difficulty The dense uniformly whitish fibrous character of this lesion is due to the fibrosis which is its predominant feature Unfortunately fibrosis of varying degrees and type is also seen in association with a number of lesions in the breast such as cystic disease or adenosis and it is not easy to identify the clinical entity *fibrous disease* of which I am writing solely on the basis of its microscopical component of fibrosis Unless the pathologist is aware that the lesion he is studying has produced a clinically evident tumor with the characteristic clinical features of fibrous disease he will probably fail to recognize it as fibrous disease and will interpret the fibrosis that

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Fig 129 Gross appearance of fibrous disease

Fig 130 Microscopic appearance of fibrous disease

he sees as a secondary feature of some more familiar breast lesion The clinical as well as the gross and microscopical features of fibrous disease, must therefore be known if it is to be identified The pathologist may get the clinical information second hand from the surgeon who palpated the tumor and cut into it in the operating room but such second hand information is not as convincing as direct evidence. The pathologist will be more easily convinced of the reality of fibrous disease if the surgeon asks him to palpate the tumor before operation and to be present in the operating room and see it as he cuts into it. Without this kind of cooperation between surgeon and pathologist fibrous disease of the breast will go unrecognized—lost in the hodge podge of "fibro-cystic mastitis Stewart is



Fig. 131 Small fibrotic lobule in fibrous disease.

one of the few pathologists who have recognized fibrous disease as a separate entity He however calls it chronic indurative mastitis

From the microscopical standpoint the 38 cases of fibrous disease in my series could be classified in three groups. The largest group constituting about half of the cases, showed both fibrosis and atrophy of the mammary lobules The fibrosis consisted of a dense thick collagenous mat, poor in cellular elements There was no evidence of accompanying inflammation in the form of lymphocytic infiltration The mammary lobules were small, and few in number (Fig. 130) They often consisted of only a few acini which appeared to be in the process of being choked off by perilobular fibrosis (Fig 131) This kind of atrophy of the lobules was seen even in the youngest patients, in whom one would expect large and active lobules Figure 132 shows this phenomenon in a patient aged 23

Fig 129. Gross appearance of fibrous disease

Fig 130 Microscopic appearance of fibrous disease

Therapy

If the surgeon could be certain of the nature of a fibrous disease tumor he might reasonably leave it undisturbed But he must biopsy it to prove its nature and to rule out carcinoma Having the lesion exposed and accessible he had best excise it, after its non malignant nature has been proved and in so doing relieve the patient of the worry that its continued presence would give her This should be done in a manner that will leave a minimal scar as I have described in my chapter on the excision of benign lesions of the breast.

Neither hormone nor irradiation therapy should be used for fibrous disease

Reference

Stewart, F W Tumors of the Breast Atlas of Tumor Pathology Section IX, Fascicle 34 Washington, D C. Armed Forces Institute of Pathology 1950

In a second and smaller group of our cases of fibrous disease the fibrosis and the lobular atrophy were accompanied by microscopic cystic disease No cases with gross cysts were included in our series of cases of fibrous disease

There was, finally, a third group of cases in which fibrosis only, without any atrophy of the lobules, was seen

What the sequence of microscopical changes leading to the fibrosis and lobular atrophy that characterize this clinical entity may be, I do not know The thought, of course, comes to mind that these changes are a special type of evolu-

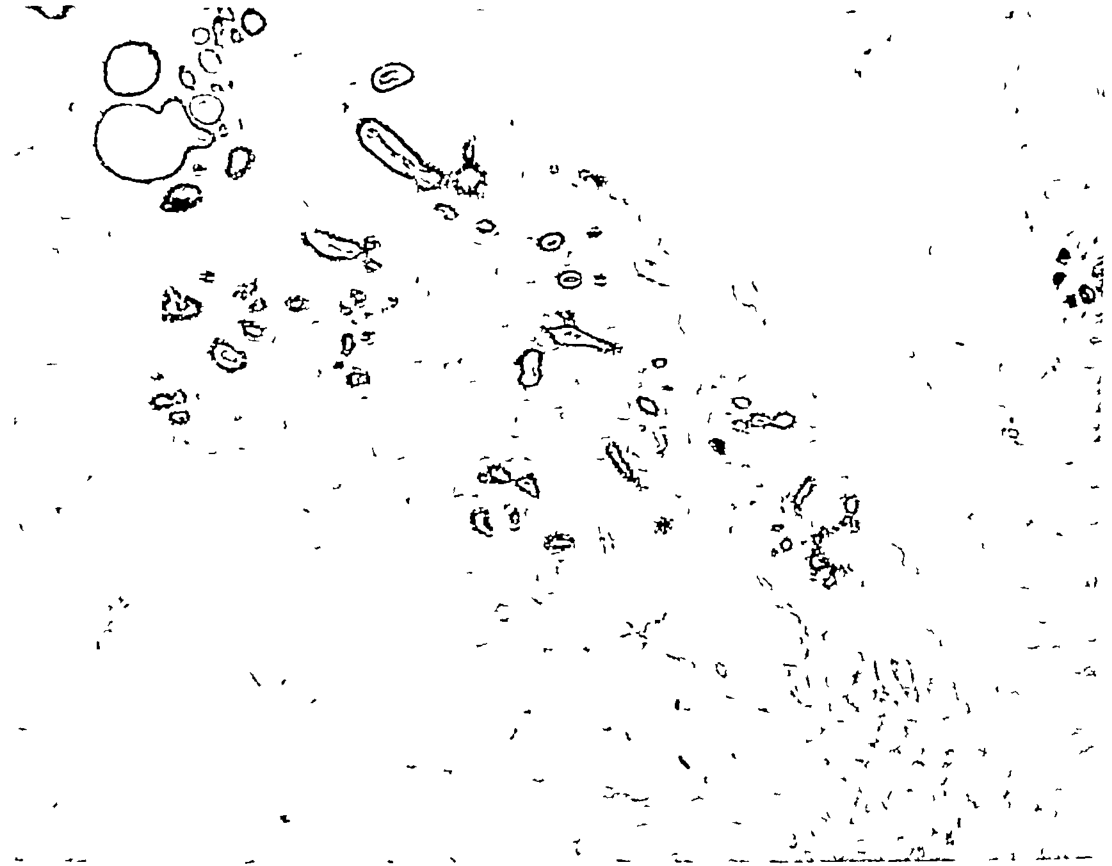


Fig 132 Atrophic lobules in fibrous disease in patient aged 23

tion of cystic disease Against this concept is the fact that gross cysts are not seen in patients with fibrous disease, either before it develops or later on in the lives of the patients who have had it It therefore seems more likely that fibrous disease is a lesion *sui generis*, which sometimes develops in association with microcysts, and perhaps as a result of related hormonal changes, but which is not consequent to, or a part of, the complex of cystic disease

Clinical Course

The fibrous disease tumor does not show much growth vigor It does not grow rapidly and does not attain a large size After it has reached 4 or 5 cm in diameter it is apt to remain unchanging I do not know what happens to these tumors after the menopause, for I have not had the opportunity of following proved lesions that were not excised

Therapy

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CHAPTER 10

MAMMARY DUCT ECTASIA

For some years, surgeons and pathologists with extensive experience with breast disease have been aware that a benign condition in the aging breast characterized by dilatation of the collecting ducts in the subareolar region, and fibrosis and inflammation around them, is a separate clinical entity It is important because its clinical picture may simulate carcinoma so closely that it has often been mistaken for it and needless mastectomy performed

The lesion has been identified by a wide variety of names Bloodgood, in 1923, wrote about it under the descriptive title of "the varicocele tumor—the clinical picture of dilated ducts beneath the nipple frequently to be palpated as a doughy worm-like mass " Adair called it "plasma cell mastitis " In so doing, he did not realize that he was describing merely the end stage of the process referred to by Bloodgood In this end stage the irritative material within the dilated collecting ducts has passed through the duct walls and set up a low grade inflammatory reaction with many plasma cells Dockerty called it "comedomastitis," and Payne and his associates labelled it "mastitis obliterans " Each of these names recalls some feature of the disease that I am describing, but none emphasizes its fundamental character as well as the term *mammary duct ectasia* that Dr Stout and I prefer to use

The disease is not well enough known to surgeons and pathologists to have won general recognition, and it is usually classified as an inflammatory process, or as one of the manifestations of that convenient catch-all, "chronic mastitis " I will describe its natural history and its pathological and clinical features in some detail, because it is important to establish it as a distinct and separate disease of the breast

The Natural History of Mammary Duct Ectasia

Mammary duct ectasia begins with dilatation of the terminal collecting ducts beneath the nipple and areola They become distended with cellular debris and lipid-containing material The dilated ducts are bluish in color and from 3 to 5 mm in diameter At this initial stage there is no accompanying inflammation There are no symptoms or clinical signs and the disease ordinarily escapes detection Surgeons and pathologists with a broad experience in breast disease know of the existence of this kind of symptomless dilatation of the terminal ducts, having encountered it while exploring the breast for other lesions

This initial symptomless form of mammary duct ectasia is more common than

is generally appreciated Frantz and her associates have recently for the first time, given us an estimate of its true frequency In an autopsy study of the supposedly normal female breasts, they found it in approximately 25 per cent of their subjects

In a small proportion of these individuals with mammary duct ectasia, the lesion evolves to the stage of producing symptoms and clinical signs We have studied 40 such cases The earliest symptom is often a nipple discharge This is yellowish or brownish but may finally become blood tinged The discharge is spontaneous and intermittent. It may be the only symptom of disease as was the case in four of our ten patients with a nipple discharge It may be of long duration in two of our patients the discharge had been present for five years

The development of a spontaneous nipple discharge necessitates surgical exploration When the surgeon exposes the base of the nipple the several dilated



Fig 133 The dilated thick walled ducts of duct ectasia

ducts are clearly seen They are bluish in color and from 3 to 5 mm in diameter The number of ducts involved by the process varies from three or four to the majority of the collecting ducts—normally some twenty-odd in number This finding is in contrast with the demonstration of a single dilated duct entering the base of the nipple in cases in which an intraductal papilloma is the cause of a nipple discharge Papillomas are not found in mammary duct ectasia

As the disease progresses the duct dilatation extends peripherally The distended ducts are strikingly defined in the as yet unchanged fatty breast stroma (Fig 133) The duct walls are greatly thickened by fibrosis and by an inflammatory infiltration of lymphocytes (Fig 134) The fibrosis within the duct walls not only thickens them but also shortens them so that flattening and, eventually retraction of the nipple, or deviation of the axis in which the nipple points develops These signs were present in 16 of our 40 patients and in 6 they were the first sign of disease Figure 135 shows nipple retraction of six months duration produced by mammary duct ectasia.

Fig 134 Higher power view of an ectatic duct showing its thick fibrosed wall.

Fig 135 Nipple retraction due to duct ectasia

Strangely enough the duct epithelium is not stimulated to proliferate In none of our cases was there any abnormal epithelial proliferation either within the diseased ducts or in the ducts or acini of the adjacent uninvolved breast tissue This absence of epithelial proliferation is one of the basic features of mammary duct ectasia Atrophy rather than proliferation of the epithelium of the involved ducts is the rule The epithelium is often so thinned out that it is barely visible in low power magnification as a thin dark line lying upon the dense collar of fibrous tissue that forms the bulk of the much thickened duct wall (Fig 136) Outside the



Fig 136 High power view of wall of ectatic duct.

fibrous collar there is usually a zone of lymphocytic infiltration separating the duct from the surrounding fatty breast stroma

The inflammatory changes in the duct walls apparently develop as a result of the irritative quality of the material with which they are distended This material is amorphous debris with characteristic crystalline bodies scattered through it (Fig 137) These are round or oval sometimes surprisingly large, and have a radial structure (Fig 138) The crystalline bodies have been identified in the dilated ducts in all of our cases and are presumably another basic feature of mammary duct ectasia that has evolved to the stage of producing symptoms and clinical signs

We have made Scharlach R stains of the material in the distended ducts and find that it stains intensely The crystals themselves however do not stain We

Fig 134 Higher power view of an ectatic duct showing its thick fibrosed wall.

Fig 135 Nipple retraction due to duct ectasia

assume from this evidence that the material is a lipid We look forward to making analytical-chemical studies of the material when we have an opportunity to collect it in sufficient quantity Lepper and Weaver have made such studies and report that the material consisted almost entirely of neutral fat

As mammary duct ectasia progresses the continuity of the atrophic duct epithelium is broken in places The irritating lipid material then sets up an inflammatory reaction in the thickened dense collagenous portion of the duct wall (Fig 139) It eventually erodes through the whole thickness of the duct wall Figure 140 shows a crystalline body and an adjacent focus of lymphocytes, lying just outside the wall of a duct

When the lipid material gets into the periductal tissues and the stroma of the breast an intense inflammatory reaction like that in fat necrosis following

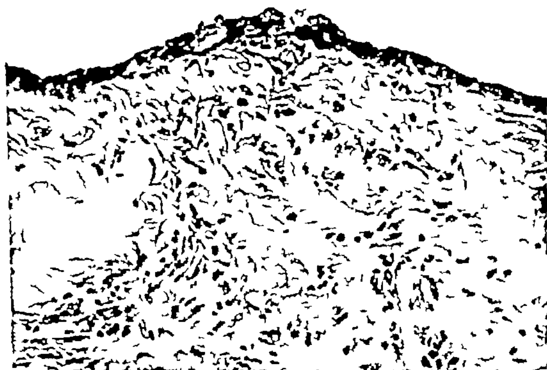


Fig. 139 Inflammatory reaction within wall of ectatic duct.

trauma, develops Phagocytic giant cells surround the lipid material (Fig 141) and histiocytes, lymphocytes, and polymorphonuclear leucocytes form a zone of granulation tissue (Fig. 142) Its center may break down and form a small cavity filled with thick yellowish or brownish material Such a lesion forms a small palpable tumor that is firm rounded and relatively fixed in the breast tissue Since it evolves from the terminal portion of the collecting ducts the tumor is almost always situated beneath the areola, or close to its edge As the inflammation and the consequent fibrosis extend, the size of the tumor increases, and it may become as large as 4 or 5 cm A tumor was palpated in 31 of our 40 patients with disease In every instance it was centrally located, either beneath or not far from the areola When the surgeon explores such a lesion he cuts into firm tissue in which there are many thick walled ducts that ooze paste like, brownish or yellowish material

Fig 137 Debris in lumen of ectatic duct

Fig 138 Characteristic crystalline body in ectatic duct

Fig 141 Phagocytosis of lipid material escaping from ectatic duct into breast tissue.



Fig. 142 Granulation tissue resulting from escape of lipid material from ectatic duct into breast tissue.

The process of duct distention, reactive inflammation, and fibrosis may eventually involve a considerable part of the breast and thus produce a tumor-like area of induration of wide extent The largest tumor in our series of patients measured 12 x 6 cm In such lesions the inflammatory reaction extends along the ducts to involve the lobules In some cases there is a predominance of plasma cells, giving the picture of so-called plasma cell mastitis Plasma cell mastitis, then, is merely a late phase of the disease we prefer to call mammary duct ectasia

Retraction signs in the form of dimpling of the skin and distortion of the contour of the breast are often seen with mammary duct ectasia at the stage at

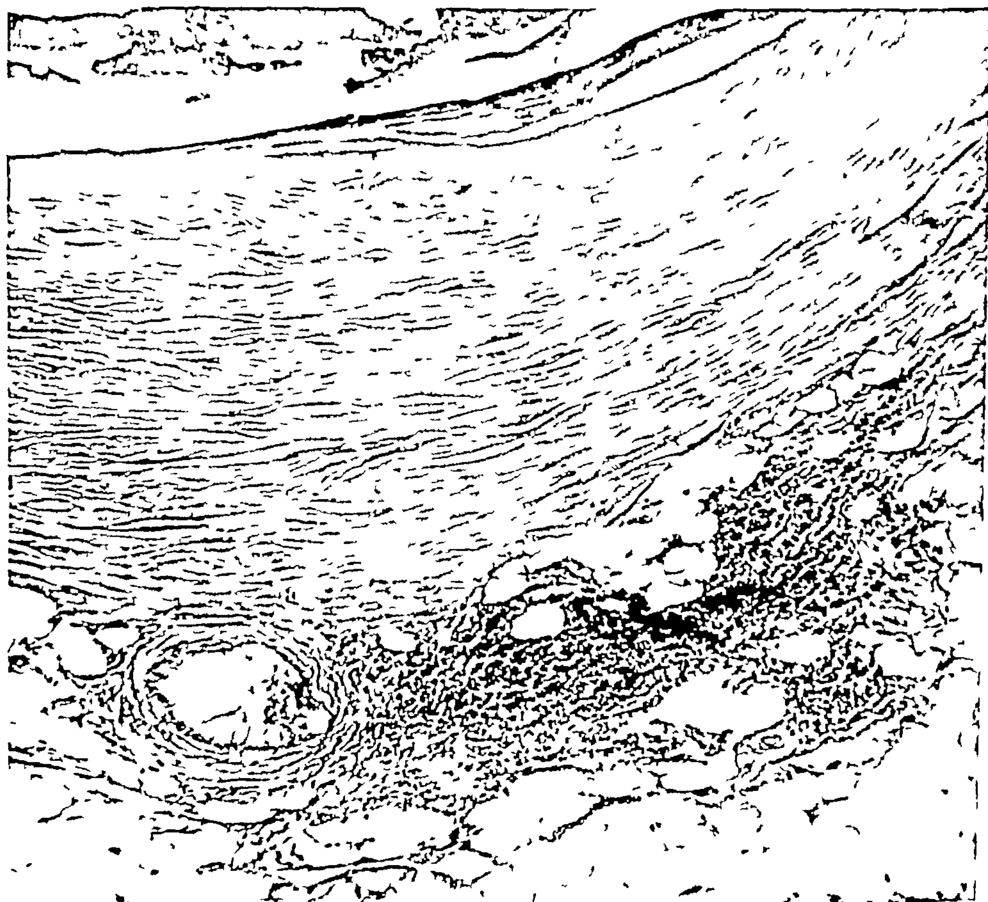


Fig 140 Crystalline body that has perforated the wall of an ectatic duct

which it produces a tumor In 15 of our 40 patients, retraction was evident on inspection, or could be elicited by molding the breast, by raising the arms, or by the use of the forward-bending position The retraction is, of course, due to the fibrosis developing in the breast stroma in the region in which the inflammation has taken place Figure 143 shows a patient with duct ectasia in whom there was marked dimpling of the skin below the left areola, when her arms were raised Her disease had produced a large tumor situated just above the areola

At one time or another during the evolution of their disease, patients with duct ectasia often have clinical signs of inflammation, such as pain or tenderness over the tumor, slight redness or edema of the overlying skin—developing and disappearing—or elevation of the body temperature Sixteen of our 40 patients had pain or tenderness, and in 12 this was the first sign of the disease noted by the

Fig 141 Phagocytosis of lipid material escaping from ectatic duct into breast tissue



Fig 142 Granulation tissue resulting from escape of lipid material from ectatic duct into breast tissue

patient Tenderness is rare in carcinoma, and pain is not ordinarily an initial symptom Four of our patients had redness of the skin over the tumor In one of them there was also a small area of edema of the skin Two other patients had localized edema of the skin Three patients had slight elevation of body temperature, up to 102° F by rectum

There is a final stage of duct ectasia in which the inflammatory process is so extensive that an abscess forms, accompanied by all the usual signs—local redness and heat, and even edema of the skin Such abscesses evolving from duct ectasia, however, are apt to be more indolent and low grade than the more common abscesses associated with lactation



Fig 143 Retraction of skin below areola caused by duct ectasia of left breast

The natural history of duct ectasia in the individual patient may be long In two of our patients nipple retraction had been present for five and three years, respectively In another patient the small subareolar tumor had been present for eight years and had begun to enlarge a month before admission

Another distinctive feature of duct ectasia is its tendency to manifest itself by repeated episodes of inflammation in the same breast, and to develop in both breasts over the course of years In most of the patients in our series the disease has been diagnosed recently and the follow-up is probably not long enough to permit any conclusion as to bilateral involvement Among our 12 patients who have been observed for more than five years, however, there were three in whom both breasts became involved One of these patients had had her right breast operated upon with findings typical of mammary duct ectasia, six years and

again two years previous to the development of mammary duct ectasia in the left breast The second patient had had her left breast removed at another hospital the presumed diagnosis being carcinoma two years before she came to the Presbyterian Hospital with a right breast tumor caused by mammary duct ectasia Review of the pathological findings in the left breast revealed that they were typical of mammary duct ectasia and that no carcinoma had been found The third patient was found to have tumors due to ectasia in both breasts when she first came for consultation The more advanced lesion in the left breast had given her symptoms for two months, and she was unaware of the small lesion in her right breast

There were also three patients in our series who had a history of repeated inflammatory episodes in the same breast due to ectasia One of them had her first subareolar abscess in her left breast when she was 45 It was successfully treated with antibiotics Six years later signs of inflammation and a small subareolar tumor developed in the same breast and local excision revealed duct ectasia The second patient had a small subareolar cyst, excised when she was 34 years old It was typical duct ectasia but went unrecognized. Nine years later a characteristic area of duct ectasia that had produced a 4 cm tumor in the same region in the same breast was excised The third patient was 50 when she had a cyst removed from the subareolar region of her right breast. Four years later another cyst was removed from the same region of the same breast The nipple was also excised at this operation The pathologist reported dilated ducts necrosis and abscess formation but did not recognize the nature of the process Two years after the second operation on her right breast she came to the Presbyterian Hospital with a tender 2 cm subareolar tumor of the left breast. It was excised and proved to be typical duct ectasia

Etiology

Mammary duct ectasia usually develops in the inactive and aging breast. In Frantz s autopsy series, the average age of the subjects with symptomless mammary duct ectasia was 61 7 years In our series of 40 cases (Chart 4) in which the lesion had evolved to the point of producing symptoms or clinical signs only ten of the patients were less than 45 years of age One of them was 26 The other nine were 34 or over Seventeen were more than 55 years of age The average age was 52 years. This evidence suggests that mammary duct ectasia is in some way related to the involution of the breasts

The disease does not seem to have any relationship to mammary function Thirty three of the 40 patients in our series had been married and all of the married patients had borne children averaging 2.8 children each The nursing history had not been adequately taken in our case histories, but the information on this point that was included did not seem exceptional In almost all of the patients who had had children the lesion had appeared many years after the last pregnancy There were only four in whom the lesion had developed within five years after the last pregnancy The shortest interval was two years The average length of time elapsing between the last pregnancy and the appearance of the lesion was twenty-one years

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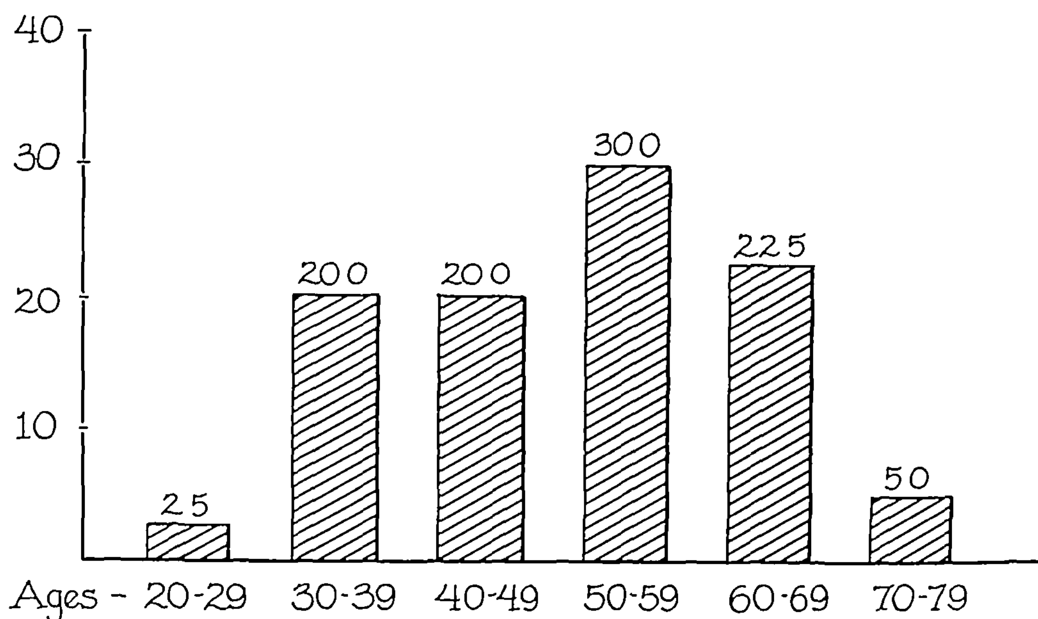
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Percentage distribution of ages in 40 patients with duct ectasia

Chart 4

group, have an abnormal menopausal history Only one had had the menopause induced artificially at an early age, when she was 36 In the remaining patients the average age at which the menopause developed was 48 years

Illustrative Case Histories

Onset with Nipple Discharge. A R , a 69 year old housewife, was admitted to the Presbyterian Hospital complaining of an intermittent brownish discharge from the left nipple of six months' duration She had borne eight children, the last thirty-two years previously, and had had her menopause at the age of 49 She had never previously had any trouble with her breasts Examination revealed no asymmetry or tumor of the left breast Pressure in the radius of 3 o'clock upon the areola produced a drop of brownish discharge from a duct in the center of the nipple A presumptive diagnosis of intraductal papilloma was made

At operation, a circumareolar incision was made between the radii of 2 and 8 o'clock When the areolar flap was dissected back to the base of the nipple, several of the collecting ducts were seen to be dilated to a diameter of 5 mm and were bluish in color They were severed at the base of the nipple, allowing the escape of yellowish fluid A pyramid-shaped sector of breast tissue surrounding the diseased ducts was then excised, the excision being carried out into the breast a distance of 10 cm

Microscopic studies showed typical mammary duct ectasia There was only minimal extraductal inflammation No intraductal papilloma or other epithelial proliferation was found

Onset with Nipple Retraction M H , a 51 year old housewife, was admitted to the Presbyterian Hospital with the complaint of retraction of the right nipple She had first noticed flattening of the nipple five or six months previously It had progressed until the nipple had recently become retracted beneath the surface of the areola She had no other symptoms She had borne two children, the last child twenty-one years previously, and had gone through the menopause at 49 years of age She had never had any breast disease

Examination showed the right nipple to be retracted to the level of the surrounding areola It could not be everted. No tumor could be palpated There was no asymmetry of the breast. With the possibility in mind that the nipple retraction might be an early sign of carcinoma, it was decided to explore the ducts at the base of the nipple

At operation, a circumareolar incision was made around the cephalad half of the areola and the areolar flap dissected up to expose the base of the nipple. The majority of the collecting ducts were seen to be bluish in color and dilated to as much as 5 mm. in diameter When cut across at the base of the nipple, they oozed thick, grayish creamy material The ducts, together with a cone of surrounding breast tissue, were excised to a depth of about 5 cm in the breast. At this level the ducts and the surrounding breast tissue appeared normal

Microscopic study of the tissue showed typical mammary duct ectasia with no intraductal epithelial proliferation and no extraductal inflammatory changes.

Onset with Tumor M R., a 46 year old housewife, was admitted to the Presbyterian Hospital complaining of tumor in the right breast of one month s duration She had no other symptoms. She had had six pregnancies with three living children, the last child having been born sixteen years previously and had nursed them all without difficulty except for a caked breast on one occasion Her periods had been regular

Physical examination showed a hard 2 cm tumor lying just beyond the edge of the areola of the right breast, in the radius of 10 o clock There was a definite shallow skin dimple over it. There were no enlarged axillary lymph nodes. A tentative diagnosis of carcinoma was made.

A circumareolar incision was made, exposing the tumor When it was incised it had the appearance of comedocarcinoma being firm and mottled pinkish gray Creamy material oozed from severed ducts. Frozen section did not show carcinoma and the tumor was therefore excised locally

Microscopic studies revealed typical mammary duct ectasia with a considerable amount of inflammatory infiltration and fat necrosis in the extraductal tissue

Onset with Pain and Tenderness A F a 39 year old housewife was admitted to the Presbyterian Hospital with a complaint of pain and tenderness in the left breast of one week's duration. She had had one child seventeen years previously and had nursed successfully She had had no previous trouble with her breasts. The pain was in the left nipple region The central portion of the breast was somewhat tender There had been no nipple discharge

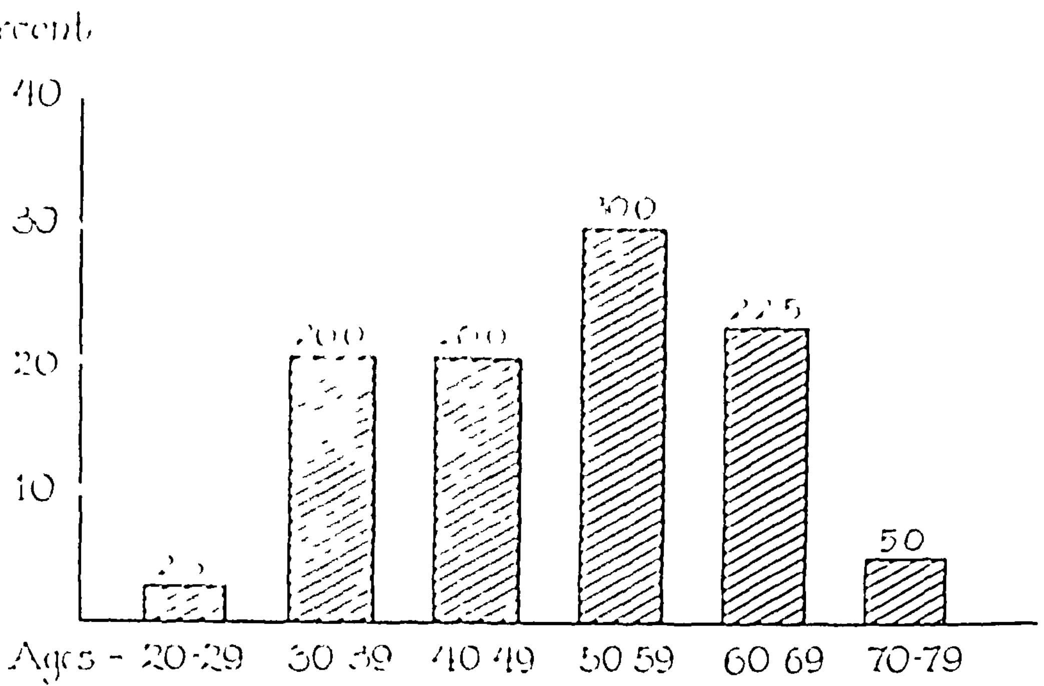
Examination revealed a poorly defined, firm area of induration measuring about 4 cm in diameter lying beneath the upper half of the areola and extending cephalad from it. There was no redness of the overlying skin or elevation of skin temperature. On palpation there was definite tenderness over the area. In the forward bending position there was slight flattening of the skin over the tumor The white blood count was 8400 with 63 per cent neutrophils Her temperature on admission was 102 F by rectum. It was decided to explore the lesion with the presumption that it was inflammatory

At operation, an incision was made around the upper half of the areola. When the lesion was cut into dilated ducts oozed creamy material At this point in the manipulations, creamy material also began to escape from the nipple. A small piece of tissue taken for frozen section showed only inflammation. The lesion was therefore excised locally

Microscopic study showed typical mammary duct ectasia with acute inflammation of the extraductal tissues

The Clinical Picture of Abscess M C an unmarried 49 year old woman, came to the Presbyterian Hospital complaining of a tumor of the left breast. Five weeks previously she had discovered a lump in the lower part of her left breast. It was slightly tender but she had thought nothing of it until four days previously at which time the skin over it had become red.

Examination showed an elevated tumor measuring 3 cm in diameter at the edge of the areola of the left breast between the radii of 3 and 5 o clock The skin over it was red and edematous *There was edema of the skin over the lower outer sector of the*



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The Clinical Picture of Abscess M C. an unmarried 49 year old woman, came to the Presbyterian Hospital complaining of a tumor of the left breast Five weeks previously she had discovered a lump in the lower part of her left breast. It was slightly tender but she had thought nothing of it until four days previously at which time the skin over it had become red.

Examination showed an elevated tumor measuring 3 cm in diameter at the edge of the areola of the left breast between the radii of 3 and 5 o clock. The skin over it was red and edematous. There was edema of the skin over the lower outer sector of the

breast. There was a poorly defined area of induration deep in the breast in this sector. There was definite retraction of the skin just below the elevated tumor at the areolar edge. There were no enlarged axillary nodes. The white blood count was 9,300, with 58 per cent neutrophils. Body temperature was not elevated.

A diagnosis of abscess of the breast was made, and the elevated mass at the edge of the areola was incised. A cavity containing 3 cc. of thick pus was entered. Deep to the abscess the breast tissue was firm. Incision into this tissue revealed dilated ducts containing pasty material. Frozen section of this tissue revealed only inflammatory changes. The indurated area was therefore excised locally.

Microscopic study showed typical mammary duct ectasia, with acute inflammation and abscess formation.

The Clinical Picture of Carcinoma. N. G., a 42 year old housewife, came to the Presbyterian Hospital complaining of a tumor in the left breast, which she had first noted one week previously. The tumor had seemed to enlarge during the week that she had been aware of it. The entire breast, including the nipple, pained her. She described the pain as burning in character. There had been no redness of the skin. She had two children, now aged 11 and 5 years, respectively. She had not nursed them because of lack of milk. During the previous two years she had been troubled with painful engorgement of her breasts before and during menstruation.

Examination revealed a hard, poorly circumscribed tumor occupying a great part of the upper central part of the left breast. It measured about 6 cm. in diameter. The tumor was fixed in the surrounding breast tissue, and the breast as a whole was somewhat abnormally fixed to the chest wall, as evidenced by the fact that its mobility over the chest wall was lessened when the pectoral muscles were contracted. In the forward-bending position there was well-developed retraction in the skin over the tumor. The skin over the upper central portion of the breast was edematous but not reddened. The left nipple was flattened, and its axis deviated upward. In the left axilla there was a firm 2 cm. node. Skeletal and chest roentgenographic studies were negative.

I made a diagnosis of carcinoma and radical mastectomy was performed without preliminary biopsy. When the breast was sectioned, the tumor was found to be made up of dense whitish tissue in which there were a multitude of dilated ducts filled with thick paste.

Microscopic studies showed typical mammary duct ectasia with accompanying infiltration. There was no carcinoma or, indeed, any form of epithelial proliferation anywhere in the breast.

Differentiation of Mammary Duct Ectasia from Carcinoma

The importance of duct ectasia depends upon the fact that it may present a clinical picture identical with carcinoma of the breast and betray the surgeon into doing an unnecessary radical mastectomy. The surgical literature, going back to the beginning of the modern pathological classification of breast disease half a century ago, contains repeated instances of surgeons with extensive experience with breast lesions who performed mastectomy for mammary duct ectasia either because they did not understand and feared the lesion, or because they thought it to be carcinoma.

A series of 8 cases in which mastectomy was unnecessarily performed for "plasma cell mastitis" simulating carcinoma was reported by Adair, in 1933. Lepper and Weaver, in 1937, described a group of 8 cases with "generalized condition of distension of the ducts of the breast by fatty secretion," in which mastectomy had been done because of supposed carcinoma. In 1941, Cromar and Dockerty reported a series of 24 cases which was seen at the Mayo Clinic during the previous thirty years. A presumptive clinical diagnosis of cancer had

been made in seventeen of the cases Simple mastectomy had been carried out in fifteen cases and radical mastectomy in nine A subsequent study of the Mayo Clinic material particularly of its pathological features was reported by Tice Dockerty and Harrington

In our clinical series of 40 cases of mammary duct ectasia from the Presbyterian Hospital a presumptive diagnosis of carcinoma was made in 25 Radical mastectomy without preliminary biopsy was unfortunately done in four I was responsible for the mistake in two in whom I thought the clinical picture to be so typical of carcinoma that I did not think it necessary to biopsy the lesion

My own distressing experience of mistaking mammary duct ectasia for carcinoma and study of the reports of other surgeons who have made the same error convince me that it is impossible to distinguish the two diseases by clinical examination When mammary duct ectasia has progressed to the stage in which inflammatory changes and consequent fibrosis have produced a tumor the clinical picture may have all the features of carcinoma The tumor is firm, poorly delimited and like a carcinoma relatively fixed in the breast tissue that surrounds it. *Retraction signs including dimpling of the skin over the tumor* distortion of the contour of the breast and retraction of the nipple, are regularly present Axillary lymph nodes, enlarged as the result of inflammatory changes are indistinguishable from lymph nodes containing metastasis

In order to emphasize the carcinoma like clinical picture of mammary duct ectasia we have summarized certain clinical features of the disease as reported by Cromar in the Mayo Clinic series of cases and from our own series of cases (Table 18)

Table 18. Clinical Features of Mammary Duct Ectasia

Clinical Features	Mayo Clinic cases (24 cases)	Presbyterian Hospital cases (40 cases)
Average age of patients, yrs	40	52
Average number of pregnancies	5	2 8
Per cent of patients with		
History of pain	79	40
Nipple discharge	21	25
Nipple retraction	42	40 ←
Tumor	100	77
Skin retraction	83	37
Enlarged lymph nodes	72	10

A past history of the appearance and regression of signs of inflammation such as *pain and tenderness or redness of the overlying skin* or the presence of these signs may suggest to the surgeon that the lesion with which he is dealing is due to mammary duct ectasia rather than to carcinoma but I do not believe that we can safely exclude carcinoma on such a basis Pain and tenderness and slight redness of the overlying skin are occasional features of mammary carcinoma.

My mistakes taught me that it is never safe to perform radical mastectomy without *microscopic proof of the nature of the lesion* There are of course, many

breast There was a poorly defined area of induration deep in the breast in this sector There was definite retraction of the skin just below the elevated tumor at the areolar edge There were no enlarged axillary nodes The white blood count was 9,300, with 58 per cent neutrophils Body temperature was not elevated

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advanced and inoperable cases of carcinoma in which the diagnosis can safely be made from the clinical picture, but all of the clinical features of earlier and operable mammary carcinoma can be produced by mammary duct ectasia Although this is a comparatively infrequent lesion, the hazard of mistaking it for carcinoma and performing a needless mastectomy is enough to justify making biopsy a rule

When a surgeon biopsies a breast tumor caused by mammary duct ectasia, his first impression is that he is dealing with the comedo type of carcinoma The cut surface of the lesion is mottled pinkish-gray and firm As he cuts across it the dilated ducts ooze creamy or pasty material A gross differentiation between carcinoma and mammary duct ectasia is impossible, but frozen section has enabled us to distinguish between the two diseases in every case in which we have resorted to it

Treatment of Mammary Duct Ectasia

When the diagnosis of mammary duct ectasia has been made by surgical exploration and frozen section, the surgeon faces the problem of choosing the proper treatment If the lesion is an early one, consisting only of dilatation and thickening of the collecting ducts, it has been our practice to sever all of these ducts at the base of the nipple, and to excise them together with a cone of surrounding breast tissue We carry the excision deeply enough into the breast to reach a level at which the ducts and the surrounding breast tissue appear normal when cut across This severance of the ducts at the base of the nipple, even though all were cut, has not had any apparent ill effects in the women in whom we have done it None of the patients in whom we have severed the collecting ducts has subsequently become pregnant, so that we have no information as to what would happen if the breast were called upon to function

In cases in which mammary duct ectasia has evolved to a more advanced stage in which periductal inflammation and fibrosis have produced a tumor, it has been our practice to excise the diseased area locally

We have closed these wounds without drainage The pus-like creamy material that oozes from the severed ducts in these lesions is not, in our experience, an indication for drainage

Since mammary duct ectasia is a perfectly benign lesion, not associated with epithelial hyperplasia, there is no justification for the surgeon doing anything more than local excision

The follow-up of these cases has not demonstrated any unexpected association with carcinoma The subsequent development of the symptoms or clinical signs of mammary duct ectasia in the opposite breast may, however, be expected in a certain proportion of patients

I am reluctant to add to the difficulty of diagnosing mammary lesions by describing a benign one that may mimic carcinoma so closely that biopsy becomes mandatory for all When a surgeon adopts such a rule, he is tempted to forego careful preoperative study of the clinical picture that mammary lesions present, since his clinical diagnosis can be only presumptive I appeal, however, for continued emphasis upon thorough study and exact recording of the clinical features of all breast lesions The intellectual discipline, which the acquisition

of these clinical facts and their correlation with the findings of pathology provide is essential to the progress of our knowledge of diseases of the breast

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CHAPTER 11

FAT NECROSIS IN THE BREAST

Fat necrosis is well known in those areas of superficial body fat that are exposed to trauma The breasts, being composed largely of fat, and so situated that they are particularly vulnerable to trauma, are occasionally the site of fat necrosis The importance of this lesion in the breast is that it simulates carcinoma in some patients, and obscures it in others

The clinical importance of fat necrosis of the breast was first emphasized by Lee and Adair in 1920 They described two cases in which a firm tumor, adherent to the skin, was diagnosed clinically as carcinoma and the breast amputated Pathological study showed only fat necrosis In one this was traced to a blow on the breast, and in the other to hypodermoclysis

There are many examples in medical history in which the first good description of a comparatively infrequent disease stimulates valuable discussion of the disease Lee and Adair's paper on fat necrosis of the breast had this result During the next decade a number of case reports were published (Cohen, Stulz, et al , Cutler, Lecène and Moulonguet Keynes, Gottesman and Zemansky, Moir, Hadfield, and Enzer) Lee and Adair, in two more papers on fat necrosis that appeared in 1922 and 1924, described a number of additional cases Since then the most important contributions to the subject have been Harbitz's description of the pathology of the lesion, and Adair and Munzer's report of their large series of 110 cases

Frequency

Fat necrosis of sufficient extent in the breast to produce symptoms that lead to biopsy is not frequent In the Presbyterian Hospital during a ten year period 1945–1955 a total of 25 patients were proved by biopsy to have fat necrosis of the breast During this same period of time more than a thousand breast carcinomas were dealt with

Age Distribution

The ages of the patients in our series of cases varied from 27 to 80 Only seven were younger than 40 Thirteen were 50 or over The predominance of older women is probably due to the fact that aged women are more apt to fall and injure their breasts

Etiology

The earlier case reports of fat necrosis featured its traumatic origin As experience with the lesion has accumulated it has become apparent that many of the

patients who have typical fat necrosis are unable to recall any definite injury In our Presbyterian Hospital series of 25 patients with proved fat necrosis only 32 per cent gave a definite history of trauma Adair and Munzer reported that 44 per cent of their 110 patients gave a history of trauma Yet it seems reasonable to assume that trauma is the cause of mammary fat necrosis in all cases except those secondary to infection or to irritating material from the ducts getting into the breast stroma as in duct ectasia Such cases of secondary fat necrosis, of course, have not been included in our Presbyterian Hospital series of 25 cases The breasts particularly in obese women are certainly often traumatized and it is not surprising that patients are unable to recall a specific injury This supposition is borne out by the fact that occasional patients with fat necrosis have ecchymosis but nevertheless give no history of trauma. There were 2 such cases in our Presbyterian Hospital series. Fifty six per cent of the patients in our series had neither a history of trauma nor ecchymosis Fat necrosis occasionally develops from surgical trauma and forms a tumor that requires biopsy One such case is included in our Presbyterian Hospital series

A strong point in favor of the traumatic origin of mammary fat necrosis is the frequency of gross or microscopic evidence of hemorrhage in these lesions Harbitz found blood pigment in all but two of the 17 examples of fat necrosis that he studied.

There are several possible explanations for the manner in which trauma produces fat necrosis The fat may be actually crushed and killed by the injury, or hemorrhage resulting from ruptured vessels may produce ischemia and necrosis

Clinical Features of Fat Necrosis

The clinical features of fat necrosis are summarized in Table 19 In the patient in whom ecchymosis is present it is the most striking feature of the lesion Figure

Table 19 Clinical Features of Fat Necrosis

Clinical Features	Adair and Munzer 1924–1946	Presbyterian Hospital 1945–1955
Number of cases	110	25
Age range	14 to 80	27 to 80
History of trauma	44%	32%
History of pain or tenderness	34%	36%
Ecchymosis of skin	22%	24%
Redness of skin	9%	20%
Tumor	100%	100%
Retraction signs	58%	52%
Enlarged axillary nodes	29%	4%
Clinical diagnosis of carcinoma	27%	44%
Unnecessary radical mastectomy	2%	0

144 shows the ecchymosis over the central area of the breast in a nurse aged 60 whom I saw twelve days after she had fallen and struck her breast. There was in addition a firm poorly delimited tumor just beyond the areolar edge at 3 o clock as indicated in the photograph by the circle It was relatively fixed in the breast tissue and measured 2 cm in diameter The ecchymosis may be relatively limited as in this patient or it may extend over a great part of the skin of the breast.

In some patients in whom there is no ecchymosis the skin over the lesion is reddened Twenty per cent of the patients in our series showed such reddening It is due to the irritative effect upon the overlying skin of the area of necrosis situated close beneath it

A characteristic feature of the majority of the fat necroses is that the lesion is situated very superficially in the breast, close to the skin This, of course, is where trauma would be expected to be the most severe

Fat necrosis may occur in any sector of the breast The commonest site, however, is the areolar region In 50 per cent of the cases in our Presbyterian Hospital series the lesion was in this region



Fig 144 Ecchymosis associated with fat necrosis due to trauma

A tumor was present in all of our cases It was usually small, the average diameter being 2 cm These tumors are firm and they are often relatively fixed in the surrounding breast tissue In these two features fat necrosis resembles carcinoma The tumor of fat necrosis occasionally has one characteristic, however, that is unusual in carcinoma This is its rounded, comparatively well delimited shape A tumor due to fat necrosis often increases slowly in size for a period of days or weeks after it is discovered This behavior of course suggests carcinoma In most cases the tumor, if not removed, eventually regresses and disappears In other patients it remains unchanged for years

Fibrosis follows the initial necrosis, and produces retraction signs In one form or another they were evident in 52 per cent of our series of cases The commonest

form is retraction of the skin over the tumor Figure 145 shows marked dimpling of the skin over an area of fat necrosis just medial to the areola in an obese woman, aged 55 with large dependent breasts Nipple retraction or axis deviation may also be produced by fat necrosis these signs were present in 5 of the patients in our series of cases

There is a type of clinical picture produced by fat necrosis that closely resembles abscess In these patients there is no history of trauma or ecchymosis The



Fig 145 Skin retraction due to fat necrosis.

first sign of disease is pain or tenderness localized over a small tumor situated usually beneath or near the areola. The skin over the lesion becomes red and warm When the supposed abscess is incised the process is found to be very superficial and comparatively localized A cavity filled with old blood or thick grayish yellow material is found Microscopical study of the wall shows only fat necrosis These lesions usually occur in obese women with large breasts and unlike the ordinary breast abscess they are not associated with lactation

Pathology

The gross appearance of fat necrosis depends upon the stage of the lesion The earliest picture is of course that of hemorrhage in an indurated area of fat. Figure 146 shows such a lesion

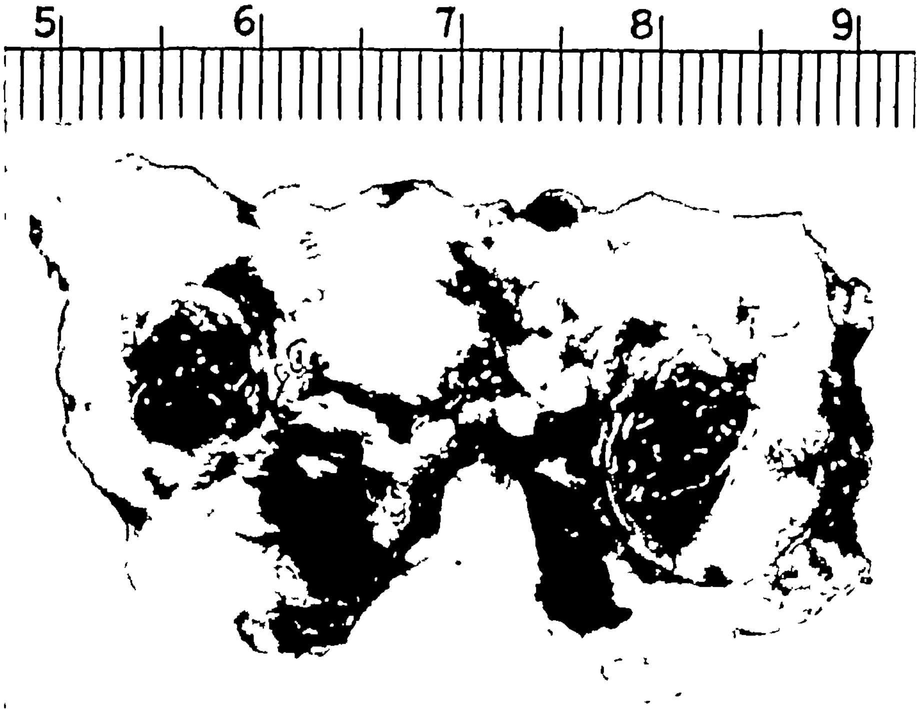


Fig 146. Gross appearance of early hemorrhagic stage of fat necrosis

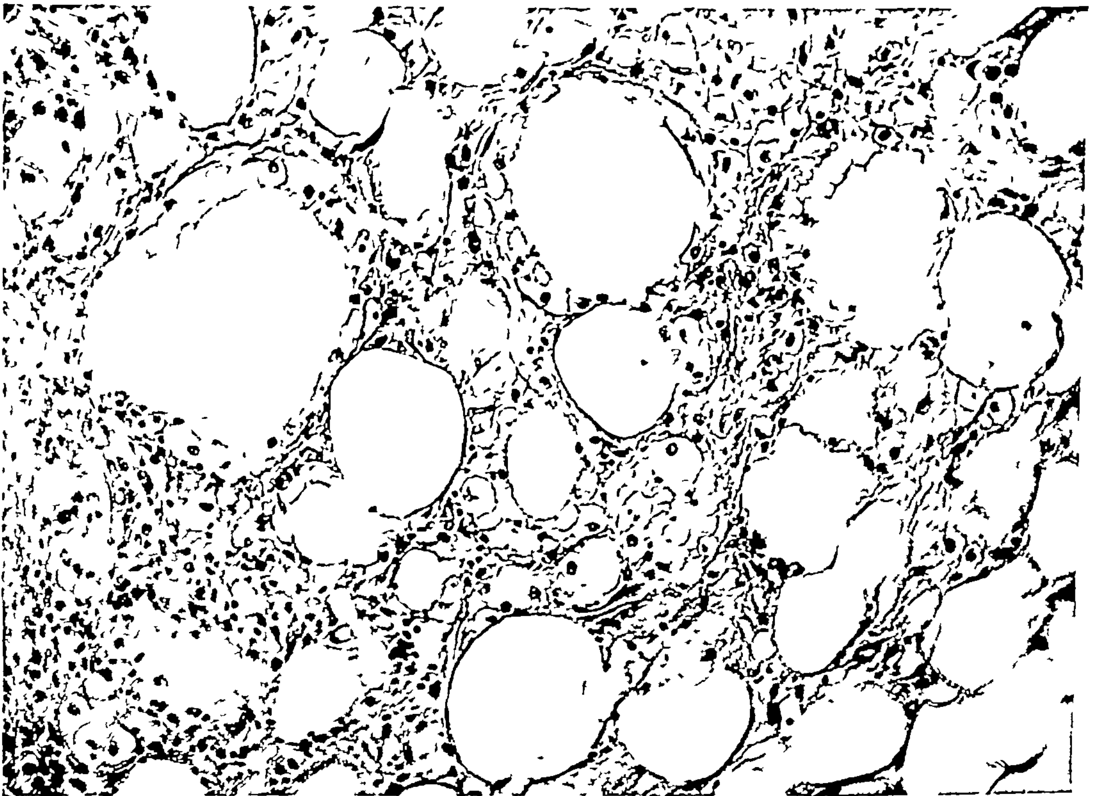


Fig 147 Microscopic appearance of early fat necrosis

After three or four weeks have elapsed the lesion forms a rounded firm tumor in the soft mammary fat Its surface is yellowish-gray with scattered dark red zones Incision into it may reveal a cavity filled with clear, oily liquefied fat, or old chocolate-colored sticky blood In other cases the necrosis produces a cavity

filled with thick grayish or yellowish necrotic material Later when fibrosis predominates, the lesion is a solid yellowish gray mass In rare cases calcification eventually occurs

Microscopically the first step in the process of fat necrosis is the dissolution and fusion of the individual fat cells to form larger vacuoles. Between the vacuoles fibroblasts lipoblasts and large clear epithelioid cells proliferate The epithelioid cells which have also been called histiocytes or clasmatocytes, or foam cells engulf the fat debris Their cytoplasms become reticulated These epithelioid cells have a tendency to line the vacuoles as they carry on their function of fat absorption Figure 147 shows these microscopical features



Fig 148 Fibrous zone surrounding central necrotic area in fat necrosis

At a later stage in the process the epithelioid cells are transformed into large multinucleated giant cells These are most often seen in the vicinity of the fatty acid crystals, oil droplets, and blood pigment that result from the fat necrosis

Fibrosis predominates at the periphery of the lesion forming a zone of denser tissue around the central area of necrotic debris Figure 148 shows this fibrous zone with the necrotic debris at the right and the surrounding fat at the left.

Eventually the area of necrosis is entirely replaced by dense fibrous tissue in which a few vacuoles filled with oil remain Figure 149 shows such a lesion eighteen months after the original traumatic fat necrosis

Diagnosis

Because fat necrosis produces a firm tumor often accompanied by skin dimpling, it suggests carcinoma. The preoperative diagnosis in twelve of the twenty five patients in our Presbyterian Hospital series was carcinoma Biopsy and

frozen section were done in all of our patients, and the nature of the lesion correctly diagnosed

A generation ago, when fat necrosis was first being recognized and discussed, it was often mistaken for carcinoma, no biopsy done, and mastectomy needlessly performed When Hadfield, in 1930, collected a series of 45 cases of fat necrosis, he found that mastectomy had been mistakenly performed in 26 per cent These were the cases, of course, in which there was no history of trauma and no ecchymosis to alert the surgeon to the possibility of fat necrosis Such mistakes will only cease when the rule of biopsy for all breast lesions is generally adopted

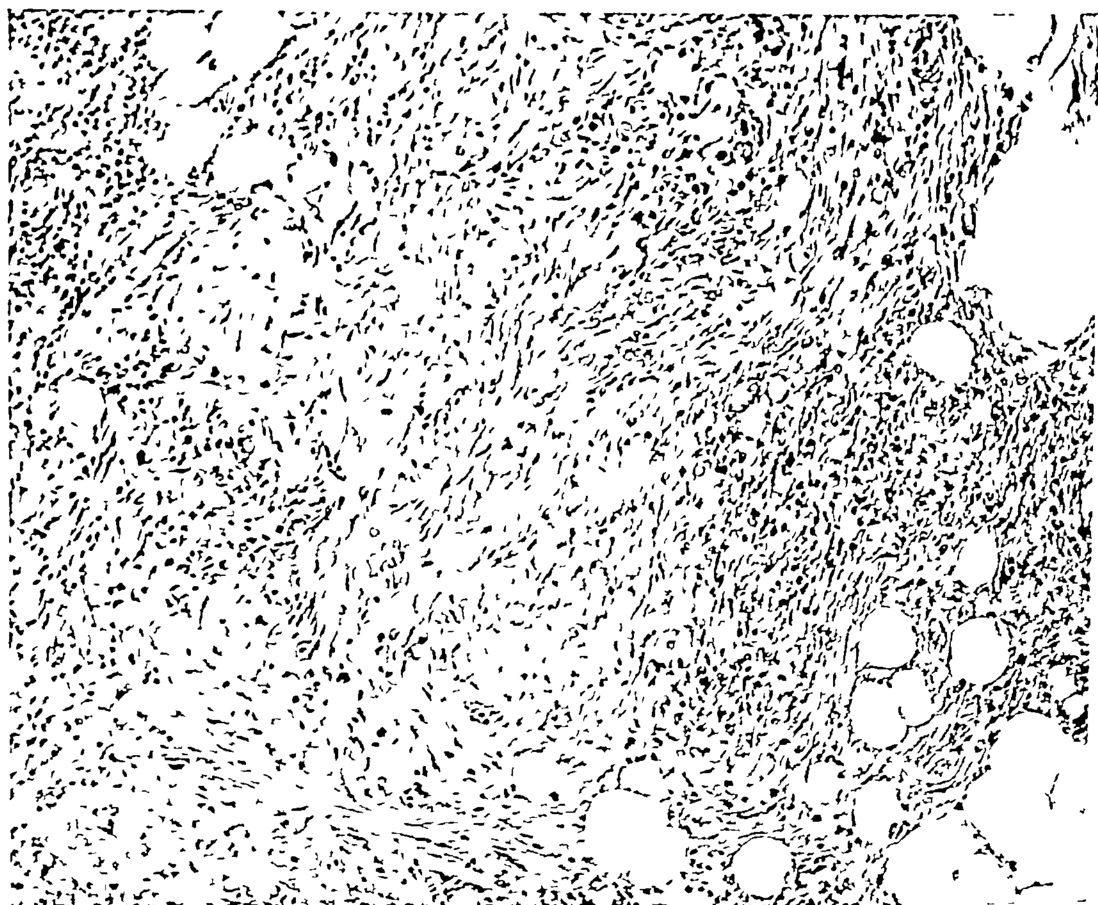


Fig 149 Residual area of fibrosis following fat necrosis

In patients who do give a history of definite trauma to the breast, and in whom ecchymosis and a tumor develop, there is danger that these signs may betray the surgeon into assuming that they are due to fat necrosis, and that it is safe not to biopsy the tumor and merely to watch it I have seen 5 patients in whom trauma and subsequent ecchymosis called attention to a tumor which proved to be carcinoma The carcinoma must have been present for some time in all 5 of these patients It would have been missed if the rule of biopsying every breast tumor had not been followed

Illustrative Case Histories

Case 1. Fat necrosis with a history of trauma and ecchymosis Mrs R O, a woman aged 60 with large pendulous breasts, fell while carrying groceries Her left breast was struck and severely bruised by a milk bottle The skin over most of the

breast became black and blue Three weeks later she discovered a lump in the breast and came for consultation.

In the upper inner sector of her breast, 4 cm. from the areolar edge there was a hard, poorly delimited 1 cm. tumor There was slight skin retraction over it At biopsy the tumor proved to be an area of fat necrosis with a central collection of old blood

Case 2 Fat necrosis without a history of trauma but with ecchymosis Mrs. A. R. a 50 year old housewife discovered a tender lump in her right breast while bathing The following day the skin over it was ecchymotic. She could not recall any injury to her breast

Examination showed a 6 cm area of ecchymosis just above the areola Beneath it there was a 3 cm firm, but freely movable, well delimited superficially situated tumor At biopsy the tumor was found to be yellowish-red necrotic fat with a central area of hemorrhage.

Case 3 Fat necrosis without a history of trauma or ecchymosis Mrs M C., an obese housewife aged 44 came to the Presbyterian Hospital because of a tumor of her right breast that she had discovered three days previously She could not recall any injury to her breast.

Examination showed a 2 cm firm tumor situated superficially just medial to the areola It was moderately well delimited and fairly movable The overlying skin was reddened and showed slight retraction There was three weeks delay in admission to the hospital for biopsy During this period the redness of the skin disappeared and the tumor grew a little larger At operation it was found to be a solid yellowish area of fat necrosis.

Case 4 Fat necrosis following surgery Mrs. G T a housewife aged 45 with large dependent breasts, was struck on the left breast by the door of a subway train. Two days later she noticed that the breast was black and blue. Two weeks later while bathing she found a lump in the region of the injury

When she was examined the ecchymosis had disappeared There was a 2 cm. firm, well delimited, movable tumor just medial to the areola of the left breast. There was skin attachment over it. At biopsy fat necrosis with a small cavity containing greenish-yellow oily fluid was found and excised. Wound healing was uneventful

Seven months later a 1 5 cm. firm, round, well delimited movable tumor was found beneath the operative scar at follow up examination. It had exactly the same clinical characteristics as the original tumor We assumed that it was a new area of fat necrosis produced by the surgical trauma Our supposition must have been correct for the tumor persists unchanged, except for slight diminution in size, fifteen years later

Case 5 Carcinoma obscured by hemorrhage following trauma. Mrs. A. G a housewife aged 54 with rather large dependent breasts, discovered a black and blue area in the skin of the inner portion of her left breast, and a lump beneath it This was four weeks after she had been struck in the same breast by a ball. She could not recall any other trauma to the breast.

When I examined her a month after she had discovered the ecchymosis, a slight residuum of it was still visible in an area of skin about 6 cm. in diameter medial to the areola of the left breast. Just at the edge of the areola there was a 4 cm. firm, poorly delimited tumor relatively fixed in the surrounding breast tissue There was slight retraction of the skin just below and medial to the tumor

I was afraid that the tumor was a carcinoma and that the hemorrhage had resulted from trauma to it Biopsy and frozen section proved me correct. Radical mastectomy was, of course, performed.

Treatment of Fat Necrosis

The treatment of fat necrosis is local excision The technique to be followed has been described in Chapter 6 In those cases of fat necrosis in which there is a cavity filled with necrotic material that looks like pus the surgeon need not fear to excise the lesion cleanly and to close the wound without drainage Special care

should be taken in these cases, however, to get the wound completely dry of blood, and to operate as gently as possible These patients, who usually have large fatty breasts, are apt to develop fat necrosis anew from the trauma of operation unless these precautions are taken

Paraffinoma

Mention should be made of the tumors of the breast that develop as a reaction to paraffin injection The practice of injecting paraffin into the tissues for cos-



Fig 150 Scarring and sinus formation in breast into which Vaseline had been injected

metic purposes has now, fortunately, been thoroughly discredited, but it continues to be done occasionally by the unscrupulous

Paraffin produces a low grade inflammatory reaction with fibrosis, and often abscess formation and the development of chronic fistulae The paraffin, moreover, often migrates in the tissues, and has even penetrated the chest wall and gotten into the pleural cavity Good descriptions of breast paraffinomas producing these complications have been presented by Krohn, by Schweitzer, by Bordet, and by Delascio

In our Presbyterian Hospital data we have a case in which Vaseline had been injected into the breast not for cosmetic purposes but for therapeutic purposes, with disastrous results

A. B a housewife aged 30 was admitted to the Presbyterian Hospital for draining sinuses of the left breast. Her first child had been born three years previously and she had nursed it successfully for three months. An abscess then developed in the left breast. Repeated incisions were required during the succeeding five months before the infection was brought under partial control During this period of time several injections of "radioactive Vaseline were made into the breast in an attempt to arrest the infection. (This therapy was not given at the Presbyterian Hospital)

Subsequent to the Vaseline injections there had been repeated flare-ups of the breast infection at intervals of three to six months Several sinuses formed which drained pus and Vaseline. Pain had led the patient to drug addiction

On examination the left breast was contracted and scarred by numerous incisions (Fig. 150) Beneath the scars were irregular firm areas of induration.

A simple mastectomy was done. When the breast was sectioned a number of greasy masses of Vaseline surrounded by dense fibrous tissue, were found There were sinus tracts from the skin leading to several of these masses. Microscopic study showed chronic inflammation with necrosis and foreign body giant cell reaction about the injected Vaseline, and much fibrosis.

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CHAPTER 12

ADENOFIBROMA OF THE BREAST

The benign nature of the general class of fibroepithelial tumors of the breast was recognized a hundred years ago by such early pioneer students of breast disease as Astley Cooper, who called them "chronic mammary tumours " But the varied microscopical pattern of this group of breast neoplasms, as it was revealed to the first few generations of pathologists who had the microscope to work with, led to a complex and confusing histological classification which, even today, handicaps us Depending upon whether the epithelial or the fibrous elements predominated, they have been called adenofibroma or fibroma When their stroma is myxomatous, they have been classed as myxoma When it is highly cellular and cystic, they have been labelled cystosarcoma, and when they appear to grow within ductlike spaces, they are called intracanalicular adenofibroma Cheatle studied the histology of these tumors in great detail and classified them on the basis of the relationship of the proliferation to the elastica layer of the ducts and acini McFarland reviewed a large number of them, deplored the confused nomenclature, and concluded that they are all varieties of a single well-characterized genus for which he preferred the name periductal fibroma Güthert suggests that this whole group of breast tumors has an organoid character, and that they arise from embryonal rests He considers the distinction of intracanalicular and pericanalicular structure an artificial one, pointing out that almost every adenofibroma shows both types of structure

The basic fact which impels us to group the various forms of fibroepithelial tumor together in one class is that they have a similar age incidence and natural history We prefer to give them the generic name of *adenofibroma* Only one special type merits discussion as a subclass—it is the giant adenofibroma, the so-called "cystosarcoma phyllodes "

Frequency

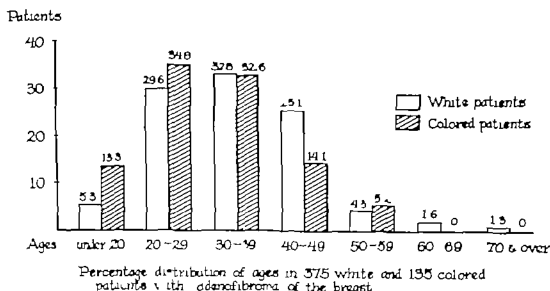
Adenofibroma is the third most common tumor of the breast in present day American females, being exceeded in frequency only by carcinoma and by cystic disease During the ten year period 1941 to 1950 a total of 440 patients with adenofibromas were studied in the Presbyterian Hospital During the same period 991 patients with breast carcinoma and 1196 patients with cystic disease of the breast were seen

The group of 440 patients includes only those in whom the adenofibroma formed a tumor which was recognized clinically Not included are a considerable

number of cases in which minute adenofibromas were found in the course of gross and histological study of breast tissue removed for other lesions An accurate appraisal of the frequency of such very small adenofibromas requires the use of microscopical sections of the whole breast Cheatle, who used this technique extensively reported that unsuspected adenofibromas, often just visible to the naked eye, occur in about 25 per cent of all normal breasts

In their study of the breasts in a series of 225 autopsies Frantz and her associates found adenofibroma in 21 or 9 per cent, of their cases Only 4 of these tumors were large *enough to be visible grossly the other 17 were found* microscopically

Adenofibroma is a disease of youth These tumors may appear any time after puberty and are the most frequent type of breast tumor seen in young women They develop somewhat earlier in colored than in white women as Chart 5



Percentage distribution of ages in 375 white and 135 colored patients with adenofibroma of the breast

Chart 5

indicates The median age for the 510 patients of both races in our series was 33 5 years In a series of 496 cases reported by Giacomelli the median age of the patients was 21 years

Racial Predilection

It is my clinical impression that adenofibromas of the breasts are more frequent in colored than in white women and our Presbyterian Hospital data tend to support this view Colored patients formed 26 5 per cent of the whole group of 510 patients with adenofibroma During the period of time in question colored patients formed only about 15 per cent of female admissions to the Presbyterian Hospital

Multiplicity

Adenofibromas are not only frequent but they are often multiple in one or both breasts In our series of 510 patients more than one adenofibroma was removed from 12 2 per cent The true incidence of *multiple tumors must have*

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The Relationship of Adenofibroma to Carcinoma

The possibility of the development of carcinoma from adenofibroma has been raised by reports such as that of Harrington and Miller Although they fail to present their evidence in any detail they state that carcinomatous transformation occurred in adenofibroma in 15 of their patients Squartini and his associates at Perugia believe, on the basis of their microscopical studies of the growth pattern of carcinoma, that some 15 per cent originate from adenofibromas

This is entirely at variance with our experience Dr Stout and I have reviewed our material and we have been unable to find a single instance of carcinoma developing *within* an adenofibroma We have a number of examples of adenofibroma and carcinoma occurring concurrently in adjacent areas of the same breast. In each of these cases the two lesions, although close to each other appeared to be quite separate and therefore presumably of independent origin This concurrent development of two independent neoplasms both frequent in the breast, might be expected in occasional patients

In the following case superficial first impression did indeed suggest that carcinoma had developed from an adenofibroma, but thorough microscopical study led us to conclude that the two neoplasms were separate and independent.

A 40 year old white housewife came to the Presbyterian Hospital complaining of hardness of the right breast of 6 months duration The breast had begun to enlarge 4 months previously

The breast contained a large, soft, well circumscribed and seemingly encapsulated, movable tumor that measured 14 cm. in diameter (Fig. 151) It was thought to be a typical giant adenofibroma. There were no enlarged axillary lymph nodes

We excised a wedge of the tumor for biopsy Grossly the tumor had a definite capsule and appeared to be an adenofibroma. Its cut surface was light brownish red, lobulated and bulging Frozen section confirmed this impression The tumor was therefore excised locally together with some surrounding breast tissue Palpation through the wound revealed several small nodules in the adjacent breast and this area was also excised

Gross study of the main tumor revealed nothing exceptional It was a typical giant adenofibroma In the breast tissue attached to it, however a number of small, firm nodules were noted The breast tissue excised separately contained several small en capsulated adenofibromas.

The microscopical structure of the main tumor was that of an actively growing adenofibroma. The stroma was cellular and its cells showed occasional mitosis There was only a slight degree of proliferation of the epithelium lining the spaces within the tumor The surprising finding was several small areas of well differentiated, predominantly intraductal, carcinoma in the breast tissue excised with the main tumor These were the firm nodules" noted in the gross examination Dr Stout studied the relation ship of the carcinoma to the adenofibroma with special care and concluded that the carcinoma, although in close contact with the periphery of the large, and some of the small adenofibromas (Fig 152) is in fact a development from the epithelium of the ducts and acini of the breast tissue between the benign tumors, and not from the adenofibromas themselves The case is one of great interest and clinical importance because of the fact that the large benign tumor almost completely filling the mammary gland completely masked the carcinoma, which was not discovered until careful path ological examination was made."

With this diagnosis it was, of course necessary to perform a radical mastectomy This was carried out according to our usual technique with a large skin graft covering the defect in the chest wall. Residual carcinoma was found in the breast tissue in the

been considerably higher, for we know that not only do small adenofibromas escape detection, but for various reasons some are not removed

Semb found adenofibroma to be multiple in 13 4 per cent of a series of 142 cases Oliver and Major reported multiple adenofibromas in 15 7 per cent of a series of 352 patients with this lesion

It is my clinical impression that multiplicity of adenofibroma is also more often seen in colored than in white patients, and our data suggest this Only 10 1 per cent of our white patients had multiple tumors, while 17 7 per cent of the colored patients had more than one tumor (Table 20) We have often seen several adenofibromas develop concurrently or successively in young colored women By the time these patients reach their thirties the disease usually loses its growth vigor No more tumors develop and those that are present no longer grow

Table 20 Multiplicity of Adenofibroma*
(Presbyterian Hospital)

	Number of patients	Number with multiple fibromas	Per cent with multiple fibromas
White	375	38	10 1
Colored	135	24	17 7
Total	510	62	12 2

Etiology

Since adenofibromas develop most frequently during youth, it might be argued that their origin is in some way associated with the estrogenic stimulation of the breast tissues during this period of life Soerensen reported histological studies of several adenofibromas that were excised after the patient had been treated with estrogen The tumors showed edema and hyperemia of the lobules, and lymphocytic infiltration

Adenofibromas may respond to the intense growth stimulus to which the breast is subjected during pregnancy Moran reported a series of ten patients in whom adenofibroma was excised during pregnancy In nine there had been growth of the tumor during the pregnancy Microscopical study of the excised adenofibromas revealed epithelial changes similar to those in the surrounding normal breast tissue

While it is no doubt a fact that adenofibromas of the breast usually show some increase in size during pregnancy, I have not observed any harmful effects of this enlargement In our patients the increase in the size of the tumor has not been great, and some of the tumors have regressed in size with involution of the breasts after completion of the pregnancy

There has been a good deal of experimental work with adenofibroma of the breast in rats, a disease to which this species is especially prone (Heiman, Wright) It is doubtful, however, that any of the conclusions concerning the etiology and natural history of adenofibroma of the breast in the rat can be applied to this tumor as it occurs in human beings

specimen. Again it was intraductal in type. There were no metastases in 15 axillary nodes.

The patient did well until seven years later when a firm, 4 cm tumor was found in the upper central portion of the right breast This was biopsied proved to be a second and presumably independent carcinoma of the contralateral breast and a right radical mastectomy performed This right sided carcinoma was, like the previous one in the left breast well differentiated and predominantly intraductal in type. There were no metastases in 18 axillary nodes.

When the patient was last seen fifteen years after her left radical mastectomy and eight years after a similar operation on her right side she had no evidence of recurrence or metastasis.

The question of the eventual development of carcinoma in the breasts of patients who had previously had adenofibromas removed is another matter We do not have adequate follow up data of patients with adenofibroma in our own clinic to provide a basis for an opinion

Semb however did not find a single instance of the development of carcinoma among 142 patients with adenofibroma followed for from four to twenty seven years after operation

Oliver and Major reported the follow up of 175 patients with adenofibroma After from four to twenty five years, only one patient had developed carcinoma.

Symptoms

Adenofibromas are usually discovered accidentally by the patient in the course of palpation of the breast while bathing or dressing These tumors rarely cause pain They are usually not tender We have not seen nipple discharge caused by adenofibroma

Physical Characteristics

Adenofibromas are usually well delimited They are rounded discoid or lobulated They may be soft, but more often have a rubbery firmness They are not hard except when calcified It is an occasional happy surprise for the surgeon to find that a stony hard tumor in an aged patient is not a carcinoma but instead a calcified adenofibroma.

The relative movability of the adenofibromas in the breast tissue in which they lie is one of their most distinctive characteristics This is due to the fact that adenofibromas do not induce proliferation of fibroblasts in the breast tissue that surrounds them Carcinoma and inflammatory lesions are immobilized by newly formed fibroblasts that fix them in the surrounding breast tissue as the guy ropes of a tent fix it to surrounding terrain

Adenofibromas do not, for the same reason produce true retraction signs False retraction the phenomenon whereby a relatively large firm tumor in a flabby breast distorts the contour of the breast adjacent to the tumor is some times seen with adenofibroma, but this phenomenon should not deceive a careful observer

Adenofibromas are usually from 1 to 5 cm in diameter When they attain a larger size and particularly when they appear to grow rapidly we put them in the cystosarcoma phyllodes subclass

Adenofibromas may develop in any part of the breast, but they are more fre

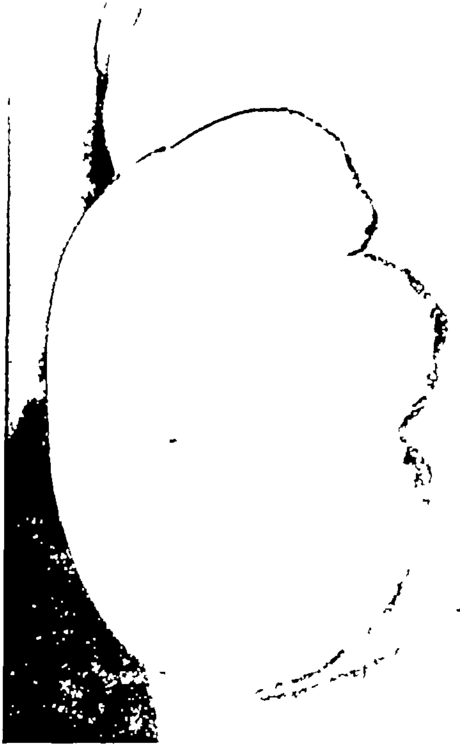


Fig 151 Giant adenofibroma with adjacent small carcinoma

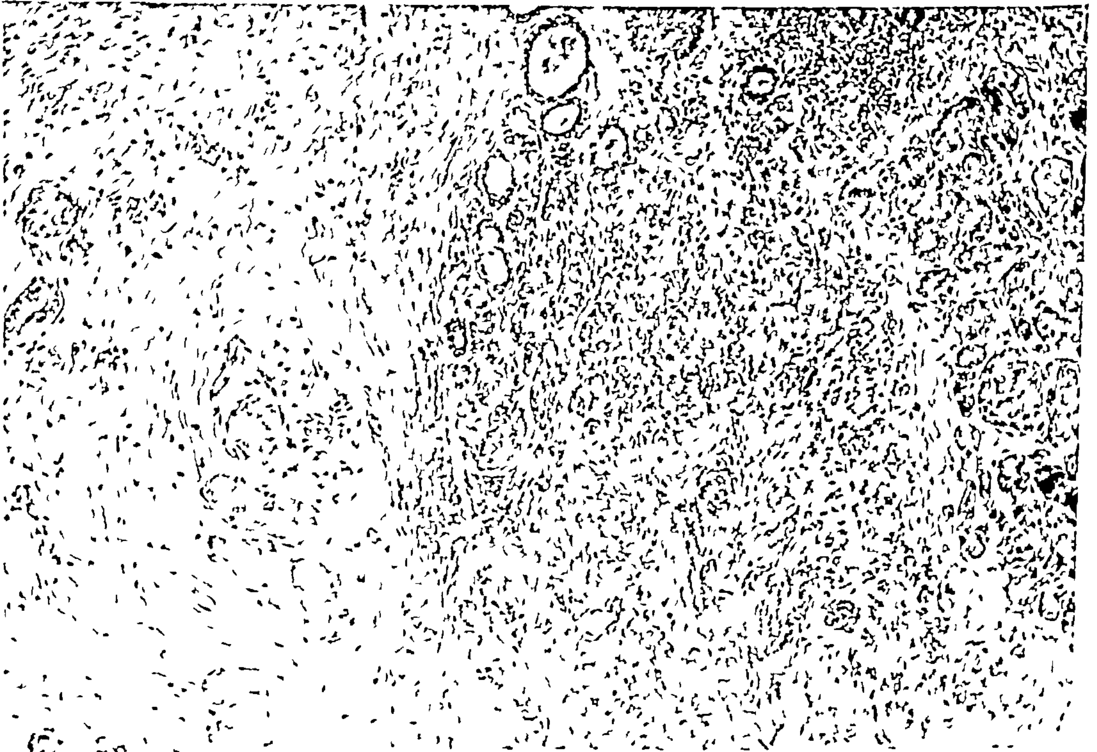


Fig 152 Adenofibroma with adjacent carcinoma

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quently situated in its upper than in its lower half, and occur most often in the outer upper quadrant

Diagnosis

An adenofibroma cannot be distinguished by palpation from a tense cyst or an area of adenosis If the patient is in her teens or early twenties, the tumor is likely to be an adenofibroma Adenosis must be considered in the differential diagnosis in somewhat older patients In women in their thirties and forties,

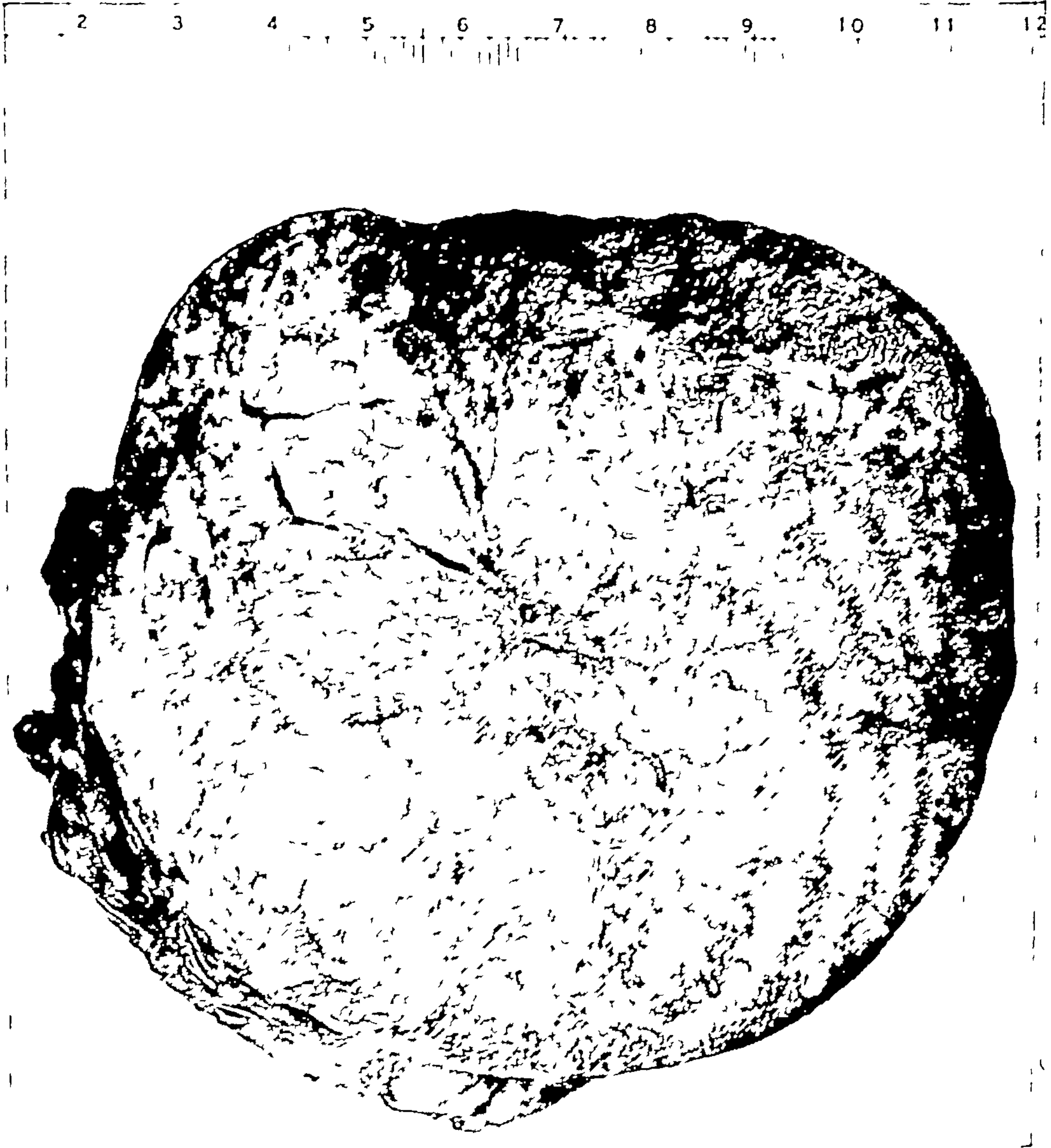


Fig 153 Adenofibroma of breast

cysts become relatively more frequent But the circumscribed type of carcinoma may mimic any of these lesions It is not safe to depend upon a tumor being an adenofibroma, no matter how typical its physical characteristics nor how youthful the patient is The patient should be told that diagnosis depends upon the microscopical findings, and that carcinoma, although unlikely, may be found, and a radical mastectomy required The diagnosis is then proved at surgical exploration under general anesthesia in the operating room with all facilities for radical mastectomy at hand, as described in Chapter 5

Pathology

The gross appearance of adenofibroma is often characteristic The tumor is so sharply delimited from the surrounding breast tissue that it seems to be encapsulated although it does not have a capsule. The cut surface is whitish resembling normal breast tissue in color As the proportion of the epithelial component in the tumor is increased the color appears more brownish red The cut surface often bulges. It frequently glistens with highlights due to the mucoid content of the tissue Figure 153 shows a characteristic adenofibroma. Clefts in the tumor are seen as dark lines and are sometimes large enough to gap open



Fig 154 Microscopic appearance of adenofibroma of breast.

Microscopically adenofibromas are made up of two components a proliferating connective tissue stroma and an atypical multiplication of ducts and acini (Fig. 154) These two components are present in varying amounts, and provide a great variety of structure Cheatle described and illustrated these variations in more detail than any other writer and explained them in terms of the site of the connective tissue proliferation in relation to the duct structure His classification in brief follows

1 Subepithelial Fibroadenoma Proliferation of the connective tissue lying just beneath the elastica and the surface epithelium of ducts and acini.

2. Pericanalicular and Periacinous Fibroadenoma. Proliferation of the connective tissue stroma which surrounds ducts and acini

3. Mixed Subepithelial and Pericanalicular and Periacinous Fibroadenoma.

The fibroblasts which form the stroma of adenofibromas usually have the characteristics of benign cells, with small, elongated, regular nuclei When the stroma of one of these tumors shows areas in which the nuclei are hyperchromatic, of varying size and shape, and with frequent mitoses, it should be classified as cystosarcoma, which I will discuss separately

The stroma of adenofibroma usually shows a degree of myxoid degeneration (Fig 155) When this myxoid change is extensive and accompanied by cystic change, the lesion is more properly placed in the cystosarcoma subclass



Fig 155 Myxoid change in adenofibroma of breast

Tumors in which the stroma shows areas of cartilage, osteoid tissue, or lipoblastic tissue, should likewise be classified as cystosarcoma phyllodes rather than as "mixed" tumors

The adenofibromas found in aged women occasionally show calcification Figure 156 shows this phenomenon in a tumor removed from a woman aged 62

The clefts of the usual adenofibroma are lined by one or two layers of inactive-appearing epithelium But the epithelial component of these tumors not infrequently shows a variety of proliferative processes, similar to those occurring in the ducts and acini of the mature breast Piling up of the epithelium within the ducts, papillary proliferation, multiplication and atypical growth of ducts, and

adenosis are all seen In our experience these epithelial changes are invariably benign

In some adenofibromas the epithelial component is so dominant that they might almost be regarded as adenomas *Figure 157 shows such a tumor*

In our material we have no example which Dr Stout is willing to classify as a pure adenoma of the breast Such tumors must be exceedingly rare It seems likely that the adenomas described by de Cholnoky and by Baker were examples of adenofibroma in which the epithelial component predominated

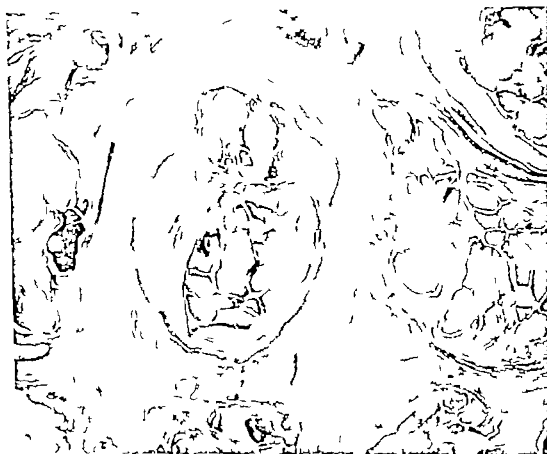


Fig 156 Calcification in adenofibroma of breast

Clinical Course

Adenofibromas may grow vigorously enough in the young women in whom they develop to reach a size of 3 or 5 cm within six months but many grow more slowly If not excised these tumors often stop growing and remain stationary with advancing age New adenofibromas apparently do not develop after the menopause the ones infrequently discovered in aged women have probably been present a long time as indicated by the frequency with which calcium is found in them

Therapy

While it may be argued that these tumors originate from some kind of hormonal disturbance it is certainly true that we have at present no understanding

2. Pericanalicular and Periacinous Fibroadenoma. Proliferation of the connective tissue stroma which surrounds ducts and acini

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even though they have the clinical features of adenofibroma, for the possibility of carcinoma becomes increasingly real beyond this age

3 Since adenofibroma is an entirely harmless lesion excision should be performed in such a way as to deform the breast as little as possible as I have described in Chapter 6

The pathologist should be asked to do an immediate frozen section upon the wedge biopsy from every presumed adenofibroma no matter how expert the surgeon and the pathologist may be at gross diagnosis. On several occasions surgeons in our hospital have excised a tumor that appeared grossly to be nothing more serious than a cellular adenofibroma, and not having asked for frozen section at the time of operation, have been shocked to learn later when the routine microscopical sections came through that the lesion was in fact a carcinoma. The distress that such errors cause both to the patient and the surgeon can be avoided by the simple rule of always doing an immediate frozen section

In young patients in whom one adenofibroma has been excised and another tumor with the same characteristics develops I have often been content to observe it. If it does not grow to such an extent that it deforms the breast it seems reasonable not to put these young patients to the expense and trouble of another operation Many such adenofibromas will remain stationary after reaching a moderate size, and they may recede somewhat in size when the patient reaches middle age. If a new tumor appears in a patient past the age of 25 who has previously had an adenofibroma excised, it should however be removed, no matter how typical of an adenofibroma it may be Beyond this age carcinoma has a significant frequency and since clinical diagnosis cannot be depended upon carcinoma must be excluded by biopsy

Cystosarcoma Phyllodes

The subvariety of adenofibroma *cystosarcoma phyllodes* is a lesion with special clinical and pathological characteristics It was named by the great German pioneer student of tumors Johannes Müller in 1838 because of the branching projections of tumor tissue into the cystic cavities within the tumor The name is a good one except for the inference of malignancy which sarcoma attaches to the lesion Müller knew that these tumors are in general benign even though their clinical course and microscopical structure often suggest that they are malignant.

This is an infrequent type of neoplasm and constitutes only about 2 per cent of adenofibromas of the breast During a forty year period, from 1912 to 1952, only 36 of these tumors were treated in the Presbyterian Hospital Lester and Stout have recently written a comprehensive study of cystosarcoma phyllodes and have reviewed the Presbyterian Hospital cases, as well as 22 cases from other clinics sent to Stout for study

The question of which of the adenofibromatous tumors to put in the cystosarcoma subclass is a difficult one Stout so classifies all fibroepithelial tumors of the breast in which there is an unusually cellular stroma suggestive of sarcoma Although these tumors are usually bulky they are sometimes removed while still small, and our data include examples as small as 2 cm in diameter

Stout also classifies as cystosarcoma phyllodes those adenofibromatous

of its exact nature Under these circumstances it is unjustified to give hormones empirically to these patients They have nevertheless often been administered, and without any effect upon the tumor

Adenofibromas should never be treated by irradiation They are highly radioresistant

The only effective treatment is surgical excision There are several principles which should be followed in carrying it out

1 The original adenofibroma should be excised, if for no other reason than to make certain of its nature Even in young patients occasional tumors which have the characteristics of adenofibroma prove on excision to be adenosis, cyst,

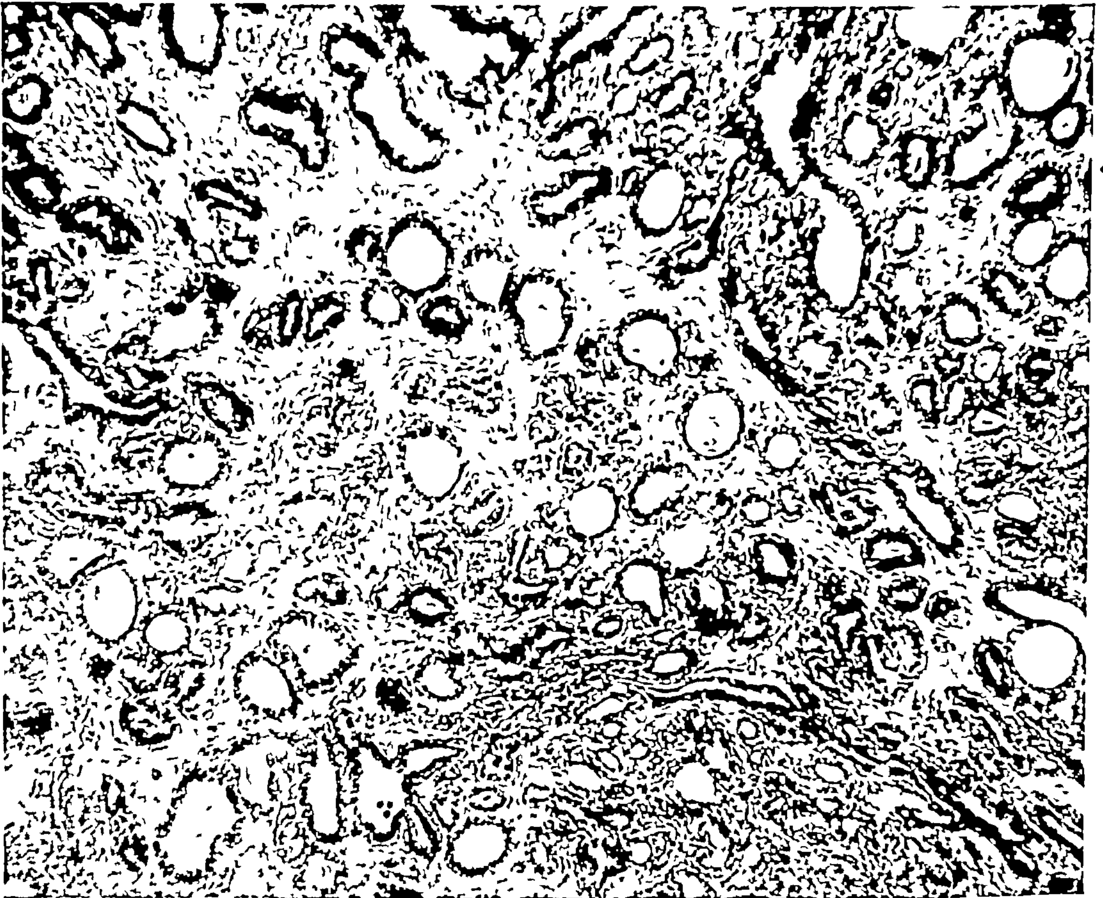


Fig 157 Adenofibroma in which the epithelial component predominates

or some other benign lesion It is of advantage to know the nature of the lesion even though it be benign Seemingly innocuous tumors will occasionally prove to be carcinoma, and correct diagnosis is vital

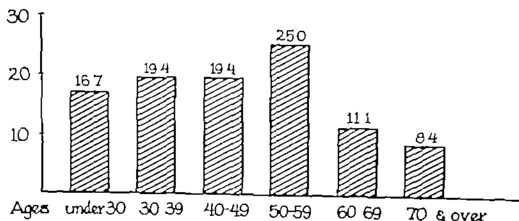
2 Since adenofibromas can in most instances be diagnosed clinically with a high degree of accuracy care should be taken to avoid needlessly frightening youthful patients In patients under the age of 25, when carcinoma is very unlikely, it is reasonable to defer operation somewhat if it is inconvenient to operate immediately The number of carcinomas for which treatment will be delayed by following this practice will be exceedingly small Only 6 out of a total of 1544 women (0 4 per cent) with carcinoma of the breast in our data were under 26 years of age In patients beyond the age of 25 tumors should be excised promptly,

its complete removal was abandoned because it would have extended the scope of the operation unreasonably

The patient moved to a southern state and was not seen until six years later At that time she was in good general health but there were two recurrent adenofibromas one measuring 3 cm. in diameter and situated at the lateral limits of the dissection on the right chest wall *presumably in residual breast tissue at this point* and another measuring 2 cm in diameter near the left sternal edge. Nothing was done about these tumors They remained stable in size while the patient went through three normal pregnancies. When the patient was last heard from twelve years after the last operation she had reached 30 years of age and the recurrent adenofibromas had not changed

Stout has carefully excluded from the cystosarcoma phyllodes class those tumors in which no epithelial component was demonstrated This is a necessary distinction because any of the usual types of sarcoma arising from cells of mesodermal origin—fibrosarcoma, liposarcoma myosarcoma etc —may develop in the breast, and these tumors should certainly be distinguished from cystosarcoma. If all types of sarcoma occurring in the breast are lumped together as Rogers and Flo for example, have recently done, the malignancy of the group is high and the comparatively benign nature of true cystosarcoma phyllodes is obscured

Cystosarcoma phyllodes occurs at a later age than ordinary adenofibroma In our series of cases, the mean age was 45 1 years (Chart 6) as contrasted with a



Percentage distribution of ages in 36 patients with cystosarcoma phyllodes

Chart 6

median age of 33.5 years for adenofibromas The youngest patient with cystosarcoma was 15 and the oldest 88 The disease developed earlier in the colored than in the white women in our series of cases

Just as with adenofibroma, there was a disproportionately large number of colored women in our series of cases of cystosarcoma. Eight or 20 per cent of the 36 patients were colored

The striking clinical feature of cystosarcoma phyllodes is a tendency to grow rapidly and to attain a great size In the majority of our 36 cases the tumor had

tumors which grow with exceptional vigor and attain a large size, although histological study of them reveals only the usual adenofibromatous pattern and no areas of sarcomalike stroma are found. It may of course be said that if enough sections were cut, such an area would be found, but this is only conjecture For all practical purposes these tumors have a benign structure

The following is an example of this type of cystosarcoma

M G, an unmarried colored girl, age 18, came to the Presbyterian Hospital complaining of a recurrent tumor of the left breast She had first noted tumors in both breasts five years previously when she was 13 years old The tumors grew to approximately 10 cm in diameter by the time she was 15 Bilateral partial mastectomy was



Fig 158 Recurrent cystosarcoma phyllodes in a girl aged 18

then done at another hospital Within a year after this operation a recurrent tumor developed on the left chest wall and grew steadily until her admission to the Presbyterian Hospital at the age of 18 Her condition at this time is shown in Figure 158

There was a large, firm but not hard, well circumscribed, lobular tumor measuring 12 cm in diameter, solidly fixed to the left anterior chest wall There were several small nodules situated both medial and lateral to the main tumor

Biopsy of the main tumor showed a benign adenofibroma without any of the histological characteristics of cystosarcoma phyllodes Through a transverse incision across the whole anterior chest wall an attempt was made to excise all remaining breast tissue on both sides, together with the recurrent adenofibroma Breast tissue was found to extend as a thin sheet laterally beyond the mid-axillary line on each side, however, and

its complete removal was abandoned because it would have extended the scope of the operation unreasonably

The patient moved to a southern state and was not seen until six years later At that time she was in good general health, but there were two recurrent adenofibromas, one measuring 3 cm. in diameter and situated at the lateral limits of the dissection on the right chest wall, presumably *in residual breast tissue at this point and another measuring* 2 cm in diameter near the left sternal edge. Nothing was done about these tumors. They remained stable in size while the patient went through three normal pregnancies When the patient was last heard from twelve years after the last operation she had reached 30 years of age, and the recurrent adenofibromas had not changed.

Stout has carefully excluded from the cystosarcoma phyllodes class those tumors in which no epithelial component was demonstrated This is a necessary distinction because any of the usual types of sarcoma arising from cells of mesodermal origin—fibrosarcoma, liposarcoma, myosarcoma, etc—may develop in the breast and these tumors should certainly be distinguished from cystosarcoma. *If all types of sarcoma occurring in the breast are lumped together* as Rogers and Flo for example, have recently done the malignancy of the group *is high and the comparatively benign nature of true cystosarcoma phyllodes is* obscured

Cystosarcoma phyllodes occurs at a later age than ordinary adenofibroma. In our series of cases, the mean age was 45 1 years (Chart 6) as contrasted with a

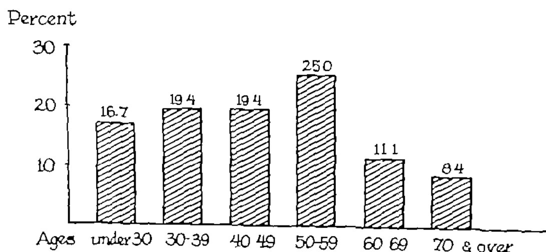


Chart 6

median age of 33 5 years for adenofibromas. The youngest patient with cystosarcoma was 15 and the oldest 88 The disease developed earlier in the colored than in the white women in our series of cases

Just as with adenofibroma there was a disproportionately large number of colored women in our series of cases of cystosarcoma Eight, or 20 per cent of the 36 patients were colored

The striking clinical feature of cystosarcoma phyllodes is a tendency to grow rapidly *and to attain a great size* In the majority of our 36 cases the tumor had

been present from one to six months Fourteen of the patients had noted recent rapid growth The tumors varied from 2 to 28 cm in diameter—21 measured from 5 to 9 cm in diameter, and 13 measured from 10 to 14 cm in diameter Figure 159 shows one of these larger tumors occurring in a 48 year old woman It had been present for eight months and measured 11 x 13 x 16 cm

These tumors are sharply delimited in the breast tissue They are relatively movable within it except when their large size distends the breast They are rounded or lobulated They do not produce retraction signs Ulceration occurs only rarely, and then in the very large tumors where pressure effect upon the overlying skin may cause it

The gross pathological features are striking The tumors are made up of varying proportions of firm opaque tissue and soft gelatinous tissue interspersed with

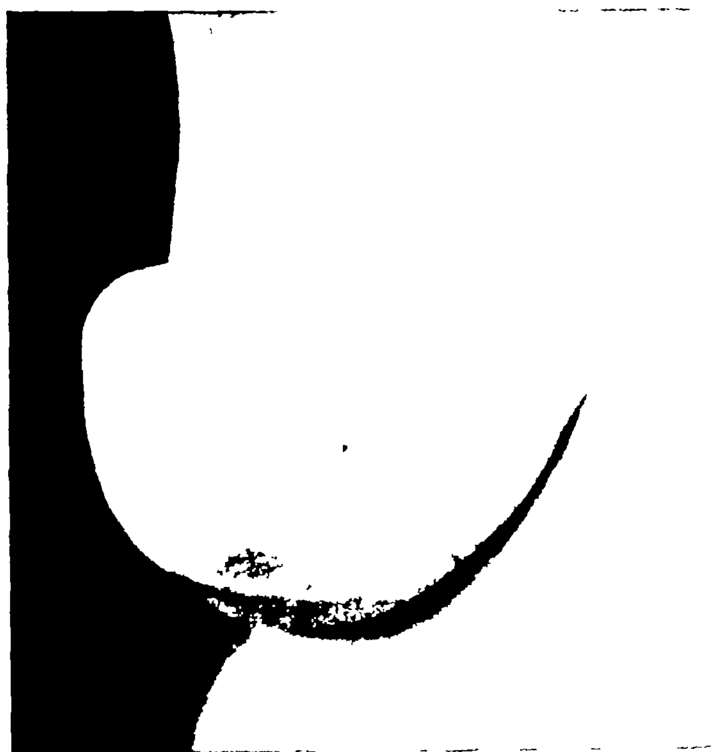


Fig 159 Cystosarcoma phyllodes in a 48 year old woman

cysts (Fig 160) The firm tissue may be coarsely trabeculated and may bulge from the cut surface The gelatinous tissue is soft and fluctuant, and yellowish, brownish, or hemorrhagic The cysts within the tumor are often filled by branch-like polypoid masses of firm tissue which project into and distend the cystic spaces, reducing them to crescentic clefts

The histological structure of cystosarcoma phyllodes shows great variation The general stromal-epithelial pattern of these tumors runs the gamut from pericanalicular cellular adenofibromas in which there are countless ducts lined by actively proliferating epithelium, through intracanalicular adenofibromas with cellular stroma and distorted ducts lined by flattened epithelium, to tumors with such marked stromal overgrowth that no epithelial component can be found in large areas

The stromal pattern in some cystosarcomas is uniformly that of well differen-

tiated sarcoma In others it is that of an anaplastic sarcoma throughout More often the stroma varies from dense, often hyalinized, relatively acellular stroma, to an anaplastic sarcomatous stroma The sarcomatoid change has a patchy distribution (Fig 161)

In many of these tumors the stroma assumes the character of a variety of mesenchymal elements Myxomatous areas are almost always seen Foci of cartilage are common (Fig 162) Lipoblastic areas may be prominent These features have led some authors unwisely to classify them as mixed tumors

The Clinical Course of Cystosarcoma Phyllodes The important question regarding cystosarcomas is whether or no they should be treated as if they were malignant. While the general opinion of the past has been that these tumors are benign several recent authors have concluded that they are not infrequently

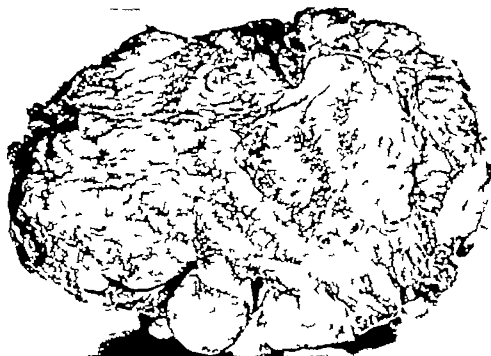


Fig 160 Gross appearance of cystosarcoma phyllodes.

malignant and that they should be treated by radical surgery The most comprehensive study is that of Treves and Sunderland, who reviewed 77 cases seen at the Memorial Hospital New York, over a twenty year period They classified 18 as malignant. Nine (13 per cent) metastasized Treves and Sunderland concluded that the best criteria of malignancy in these tumors is not their gross size but rather the presence of microscopic areas of focal subepithelial stromal cellularity and anaplasia The presence of bizarre giant cells in an otherwise benign appearing stroma was not, in their experience, an indication of malignancy

Stout and Lester attempted to apply the Treves and Sunderland criteria of malignancy in the 58 cases available to them for study They found, however, that only 2 of their 5 metastasizing tumors could be classed as malignant by these criteria They concluded that it is unsafe to rely for therapeutic guidance upon these criteria as applied to biopsy specimens The malignant appearing area in one of these truly malignant cystosarcomas may be so small that only

Fig 161 Sarcomatoid area in cystosarcoma phyllodes (Lester and Stout, Cancer, Vol 7, 1954)

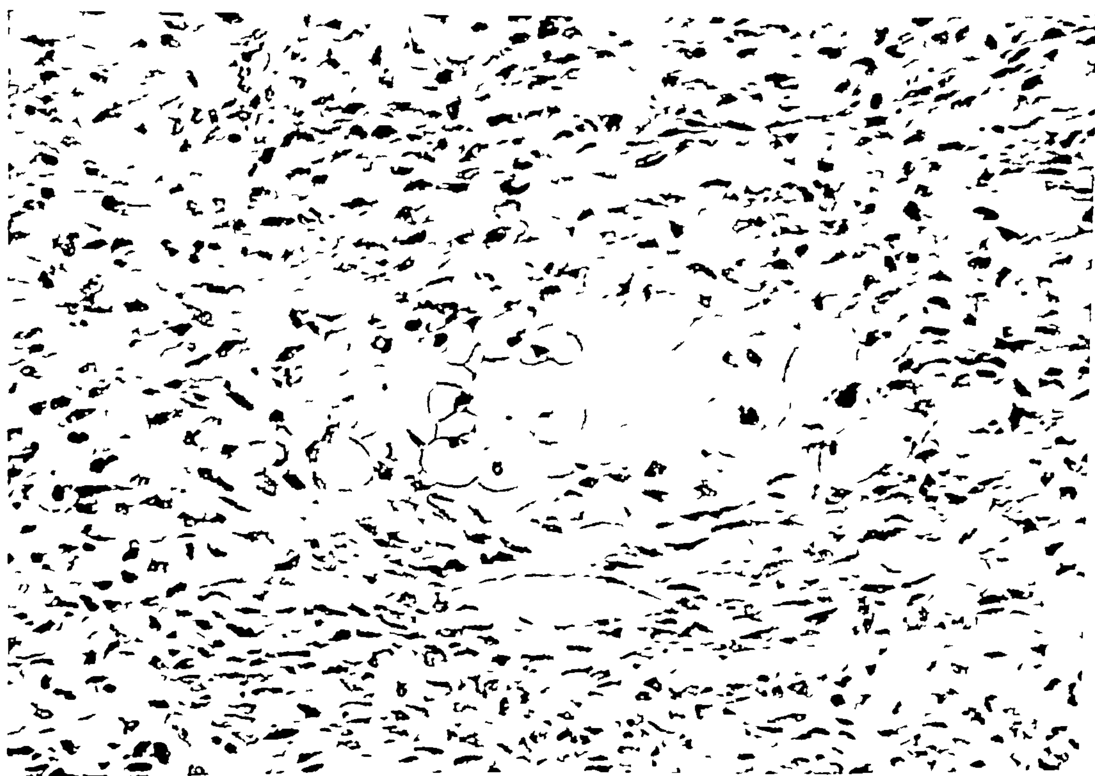


Fig 162 Area of cartilage in cystosarcoma phyllodes (Lester and Stout, Cancer, Vol 7, 1954)

meticulous study of many sections from the entire tumor will find it On the other hand, many cystosarcomas will be found to contain highly malignant appearing stromal areas, yet their clinical course is entirely benign

It seems likely that the high proportion of malignant tumors (13 per cent) in the Memorial Hospital series of cystosarcomas is due to the fact that that clinic,



Fig. 163 Malignant cystosarcoma phyllodes.

because of its reputation as a cancer hospital, attracts an abnormally high proportion of patients with unusual malignant disease Indeed, Treves and Sunderland themselves admit the suspicion that their series has been overweighted with malignant cases

The Presbyterian Hospital data would seem to represent more truly the real incidence of a malignant course in cystosarcoma for these data represent the

experience of a general hospital where there is no artificial concentration of unusual clinical material Only one of our 36 tumors (2 8 per cent) is known to have metastasized This case was so unusual that I will describe it in detail.

S H, a 50 year old nulliparous Negress, was admitted because of a rapidly enlarging breast tumor present for 4 months, with ulceration noted two weeks previously The left breast was enormous, and showed a small area of ulceration over its most protuberant portion (Fig 163) Simple mastectomy with removal of low axillary nodes was performed The specimen weighed 8 pounds The tumor was lobulated and circumscribed The cut surface presented a mixture of firm, white, whorled tissue with multiple cysts, large gelatinous areas, and foci of hemorrhage and necrosis

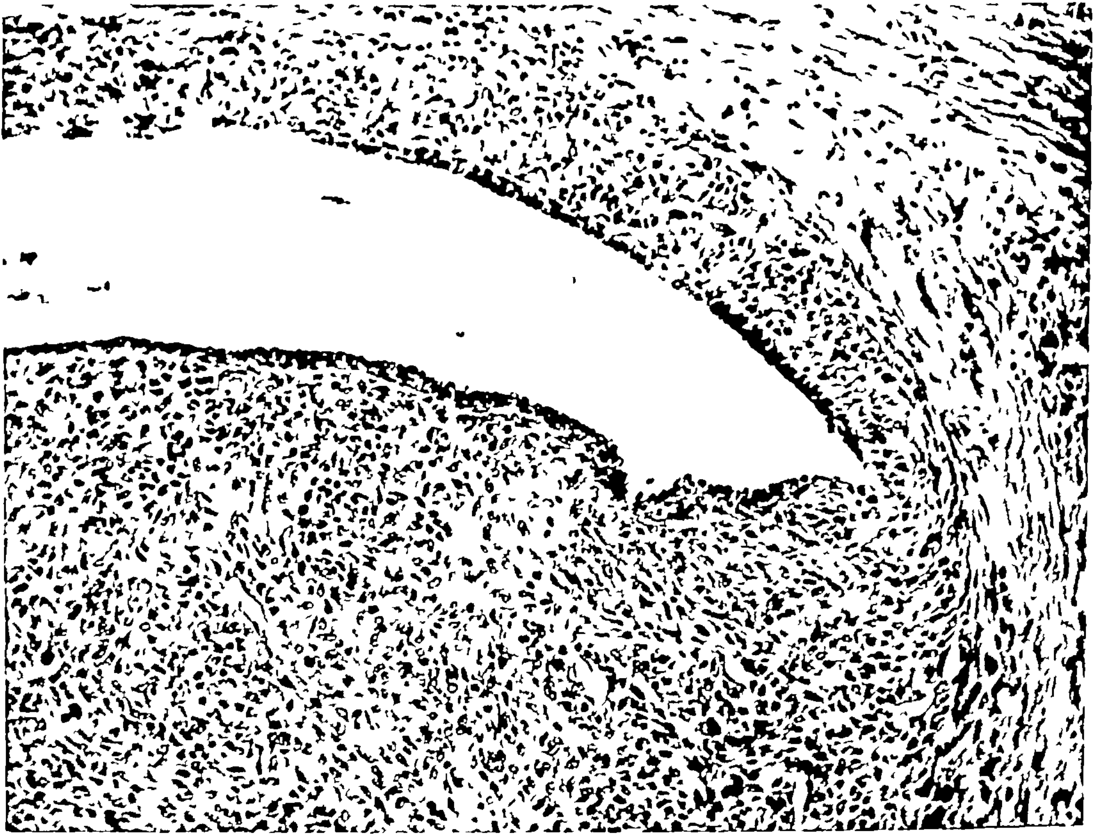


Fig 164 Cellular area from malignant cystosarcoma phyllodes.

About two months later she returned with partial intestinal obstruction due to intussusception produced by multiple polypoid tumors in the small intestine At this time a laryngeal tumor and large cervical nodes were noted and biopsied Segments of gangrenous bowel were removed She died seven months after the discovery of her breast tumor, with generalized peritonitis, a sequel of the intestinal gangrene

Multiple sections of the original breast tumor showed the pattern of an intracanalicular fibroma with many compressed and distorted ducts lined by uniform epithelial cells in a moderately cellular stroma, portions of which were dense while other portions were myxomatous Occasional mitoses were encountered but there was no significant degree of pleomorphism There were large foci of hemorrhage and necrosis A single section among numerous additional ones made from the original tumor after its malignant clinical course had become evident, contained an unusually cellular focus composed of large spindle-shaped and polygonal cells with variation in nuclear size and staining and moderate amounts of deeply-staining cytoplasm (Fig 164) Occasional giant forms and numerous mitotic figures were seen

Many of the multiple small intestinal tumors were polypoid (Fig 165) and one such

tumor formed the head of the intussuscepted segment. These tumors one of which is shown in Figure 166 as well as biopsies of the laryngeal tumor and of a cervical mass, presented a similar microscopical picture. They were vascular cellular tumors with large spindle-shaped cells containing ovoid, vesicular nuclei which varied considerably in size and shape. In some areas the cells tended to be rounded or polygonal resembling those seen in the cellular focus in the primary breast tumor

At postmortem examination similar metastatic lesions were found in the heart lungs, stomach, intestinal tract and cervical region Tumor was not found in any lymph nodes. Tissue from the cervical region removed operatively and at autopsy could not be identified as nodal in origin. Epithelial elements were not found in any of the metastatic deposits

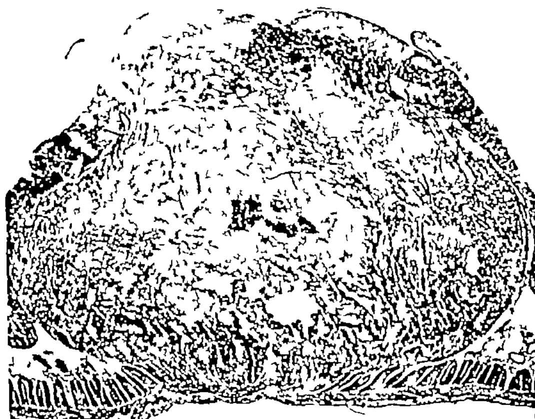


Fig 165 Polypoid metastasis to ileum from malignant cystosarcoma phyllodes—low power view

This huge rapidly growing, fibroepithelial breast tumor produced widespread visceral metastases and killed the patient within a year Histologically the major portion of the tumor had the structure of a fibroadenoma with moderately cellular but quiescent stroma Only the connective tissue elements were represented in the metastases as an anaplastic sarcoma similar to that seen in one small portion of the original breast tumor

The other 35 cases in our Presbyterian Hospital series were clinically benign Nine of these tumors contained areas of anaplastic stromal cells which Stout classed as histologically malignant, yet they were controlled by limited surgery The following case is an example of this group

L S a 61 year old white housewife came to the Presbyterian Hospital complaining that a tumor which had remained unchanged in her right breast for forty two years

Fig 166. Metastasis of malignant cystosarcoma phyllodes to ileum—high power view

Fig 167 Focus of sarcomalike cells from benign cystosarcoma phyllodes

had begun to enlarge one month previously Examination showed a well circumscribed, lobulated movable tumor 9 cm in diameter in the outer half of the right breast. There was no retraction It was biopsied proved to be a cystosarcoma, and excised locally through a curved lateral incision Microscopically it had the pattern of an adenofibroma except for several areas where foci of anaplastic spindle-shaped cells varying considerably in size and shape, and containing frequent mitoses (Fig 167) The patient was perfectly well eight years later

Our Presbyterian Hospital experience has led me to regard cystosarcoma as benign and to treat it by simple excision It is probably wise to remove a margin of the surrounding breast tissue but I see no need for removing the breast

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CHAPTER 13

INTRADUCTAL PAPILLOMA

The papillary neoplasms of the breast continue to present one of the most difficult diagnostic and therapeutic problems that surgeons face There are two main types of papillary lesions—the benign intraductal papillomas which are relatively frequent, and the malignant papillary carcinomas, which are rare Both give rise to a serous or bloody nipple discharge These two lesions, so different in their prognosis, have often been confused. The key to this confusion is the same as for most other breast neoplasms namely close correlation of the clinical features of these tumors with their pathological characteristics

In the present chapter I shall deal with the benign intraductal papillomas. The malignant papillary carcinomas will be discussed in Chapter 22.

J Collins Warren in a paper which he wrote in 1905 presenting a new classification for benign tumors of the breast and emphasizing the necessity for closer cooperation between pathologist and surgeon was one of the first to recognize the benign character of "papillary cyst adenoma, and to recommend that the surgical attack on these lesions be limited to local excision Earlier observers had often regarded these lesions as malignant, and had used a variety of terms to describe them—adenocystoma papilliferum mammae, villous papilloma, papillary fibroma, duct papilloma, cysto-adenoma intracanaliculare, proliferous cysts or carcinome villeux. Warren reported 9 cases of intraductal papillary cysto-adenoma from the Massachusetts General Hospital 6 of which were treated successfully by local excision

Greenough and Simmons in 1907 made another study of the Massachusetts General Hospital data and reported 20 cases of papillary cysto-adenoma. In 17 patients the lesion was benign Seven of these patients had simple mastectomy and the remaining ten had local excision The follow up of this group of patients was not complete, only one of them being followed for as long as four years Nevertheless, Greenough and Simmons believed that they had sufficient evidence to conclude that papillary cysto-adenoma ordinarily requires only local excision.

In 1916 Dean Lewis, of Chicago in a discussion of bleeding nipple emphasized that a discharge of serum or blood from the nipple was usually indicative of benign intraductal papilloma and not of carcinoma He advised operative search for and excision of the papilloma, even when no tumor could be palpated He pointed out that in these cases the situation of the papilloma could be determined by the appearance of the discharge when pressure is made over it Lewis believed that local excision sufficed for intraductal papilloma, and that in the

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benign papillary cysto-adenomas eventually developed into papillary adenocarcinomas

In their book published in 1931 Cheatle and Cutler presented elaborate histological evidence in support of their belief that benign papillomas may evolve into carcinoma They did not include any convincing clinical evidence in support of this belief Nevertheless they advocated simple mastectomy as the proper treatment for papilloma

Saphir and Parker in 1940 made an interesting study of the papillary lesions of the breast They studied 58 intraductal papillomas and divided them into three groups. Forty two were placed in Group I and designated as the fibrous type nine were placed in Group II and called the glandular type and seven were placed in Group III and termed the transitional type They regarded the first two groups as well differentiated tumors and benign but felt that the latter group which was not glandular in structure being made up of more or less solid masses of cells without connective tissue stalks was potentially malignant

In 1941 Gray and Wood again reviewed the experience at the Mayo Clinic regarding discharge from the nipple Eighty-eight patients with a serous or bloody nipple discharge proved to have benign papilloma Simple mastectomy was carried out in almost all of these cases In 87 other patients with a serous or bloody nipple discharge a diagnosis of malignant papilloma was made The details of the clinical signs in these patients with presumed malignant lesions are not given beyond the fact that 52, or 60 per cent, had no palpable tumor The diagnosis of carcinoma was based upon the microscopic findings It is of interest to note that the Mayo Clinic pathologists classified the lesions in 44 of these 52 patients as Grade I adenocarcinoma This fact, and the photomicrograph which Gray and Wood include of one of these tumors leads us to believe that they were only benign papillomas

Estes and Phillips have recently (1949) studied a series of 87 cases of intraductal papilloma seen in their clinic and conclude that simple mastectomy is the proper treatment although none of their patients treated by local excision subsequently developed carcinoma

It is the tendency to employ a comparatively radical method of treatment for what is in our opinion a benign breast lesion that stimulated Dr Stout and me to review our experience with intraductal papilloma in the Presbyterian Hospital and to present it in a paper in 1951 The data in the present chapter are largely derived from that study

We reviewed all the intraductal papillomas recorded in the Presbyterian Hospital and the Laboratory of Surgical Pathology of the College of Physicians and Surgeons for the years 1916 to 1941 inclusive There were 367 hospital records 14 of which had insufficient data for tabulation leaving 353 for further consideration

In studying the benign papillary lesions of the breast it is necessary at the outset to divide them into two groups of cases (Table 21) The first group consists of the cases of intraductal papillary proliferation discovered only in microscopical study of breast tissue removed for other lesions No grossly visible papilloma was found

These microscopic papillomas do not in themselves constitute a separate

occasional case in which malignant transformation occurred this change could be detected from the gross appearance of the lesion

Miller and Lewis, in 1923, reviewed their experience with 40 patients with a serous or bloody discharge from the nipple and found it was due to benign intraductal papilloma in 32 per cent, and to carcinoma in 68 per cent This predominance of cases of carcinoma led Lewis to take a more grave view of nipple discharge than he had presented in his earlier paper He emphasized that a serous or bloody nipple discharge is evidence of a pathological lesion which should be searched for and identified

In 1917 Judd reviewed the Mayo Clinic records of 100 patients with serous or bloody nipple discharge, and reported that 57 per cent were proved to have carcinoma All the patients with carcinoma had a palpable breast tumor, a fact which led Judd to use the presence of a tumor as a distinguishing feature between nipple discharge due to carcinoma and nipple discharge due to intraductal papilloma None of Judd's intraductal papillomas formed a palpable tumor He therefore advocated mastectomy for all patients with nipple discharge and a palpable tumor, but conservative treatment for those in whom no tumor could be detected

Joseph C Bloodgood was another contemporary student of breast neoplasms who discussed intraductal papilloma in a series of papers (Bloodgood, 1921, 1922, 1932) He regarded it as a relatively innocuous lesion He did not think it precancerous In his opinion a serous or bloody discharge was ordinarily due to intraductal papilloma—not to carcinoma In his series of cases of carcinoma of the breast a discharge from the nipple was noted in only 1 per cent prior to the palpation of a breast tumor

In 1927 Deryl Hart reviewed the Johns Hopkins' data concerning "intracystic papillomatous tumors of the breast, benign and malignant," and wrote one of the best available papers on the subject He studied 95 cases with benign papillary lesions and 24 malignant ones Forty-eight per cent of the benign lesions had a nipple discharge, which in a relatively large number had been present for many years In 20 per cent no tumor was palpable Local excision sufficed for cure of these benign papillomas

A nipple discharge occurred in only 12 5 per cent of Hart's cases with malignant papillary lesions The duration of symptoms was usually short A tumor was present in every malignant lesion, and in most cases the clinical picture suggested malignant disease Hart emphasized the necessity of carrying out radical mastectomy for these malignant lesions

In Hart's series there was only one case in which the clinical history suggested that a benign papillary lesion had transformed into a malignant one

Adair (1930) presented a very different point of view He reviewed 108 cases of sanguineous discharge from the nipple, and reported that in 47 2 per cent the symptom was due to malignant and in 52 8 per cent to benign lesions Forty-nine out of 57 benign lesions were classified as intraductal papillomas or papillary cysto-adenoma, and 17 out of 49 carcinomas were classified as papillary adenocarcinoma Adair concluded that a serosanguineous or bloody discharge signified the presence of a carcinoma about as often as it did a benign lesion, and that

Incidence

Frequency During the 1916–1941 period during which 110 intraductal papillomas were admitted to the Presbyterian Hospital, approximately 1,450, or 13 times as many carcinomas of the breast were admitted The papillomas are, therefore in a comparative sense a relatively infrequent lesion During a 12 year period (1943–1954) I saw in private practice almost the same ratio of proven intraductal papillomas and carcinomas 44 of the former and 546 of the latter

Age The ages of our patients with intraductal papilloma had a wide range (Chart 7) the youngest being 19 and the oldest 82. Their mean age was 45.3 years, or slightly younger than the mean age of our Presbyterian Hospital patients with breast carcinoma which was 50 years

Racial Predilection

There was no evident racial predilection for intraductal papilloma in our data.

Multiplicity

Grossly visible intraductal papillomas are infrequently multiple in one breast, and they may develop as single or multiple lesions successively in both breasts I have seen several patients in whom a single intraductal papilloma was excised from a central duct in one breast, and the same phenomenon occurred in the other breast some years later

The following is an extreme example of the multiplicity of the disease.

E.H., a Negro housewife aged 49 came to the Presbyterian Hospital complaining of a bloody discharge from both nipples Twelve years previously she had first begun to have a discharge from her right nipple, and a year later from the left one. As time went on the discharge became more copious from the right breast. It was increased during menstruation.

Examination of the right breast revealed a 1 x 0 5 cm. well delimited movable tumor beneath the edge of the areola in the radius of 12 o clock Pressure over this tumor produced a discharge of bloody fluid from the right nipple. There was no tumor in the left breast and no discharge could be elicited from it.

The surgeon in charge of the patient did a bilateral simple mastectomy Pathological examination of the right breast showed that the subareolar tumor was an 8 mm. friable, intraductal papilloma, attached by a single stalk to the wall of a dilated duct. Other small papillomas were found widely scattered throughout the duct system.

Pathological examination of the left breast showed numerous small papillomas widely scattered throughout the duct system of this breast also Microscopically all the papillomas were benign.

This type of extensive involvement of both breasts by benign papillary disease is rarely seen In our experience, most of the papillary lesions which are wide spread in the breast and which involve a large area of its periphery prove to be papillary carcinomas

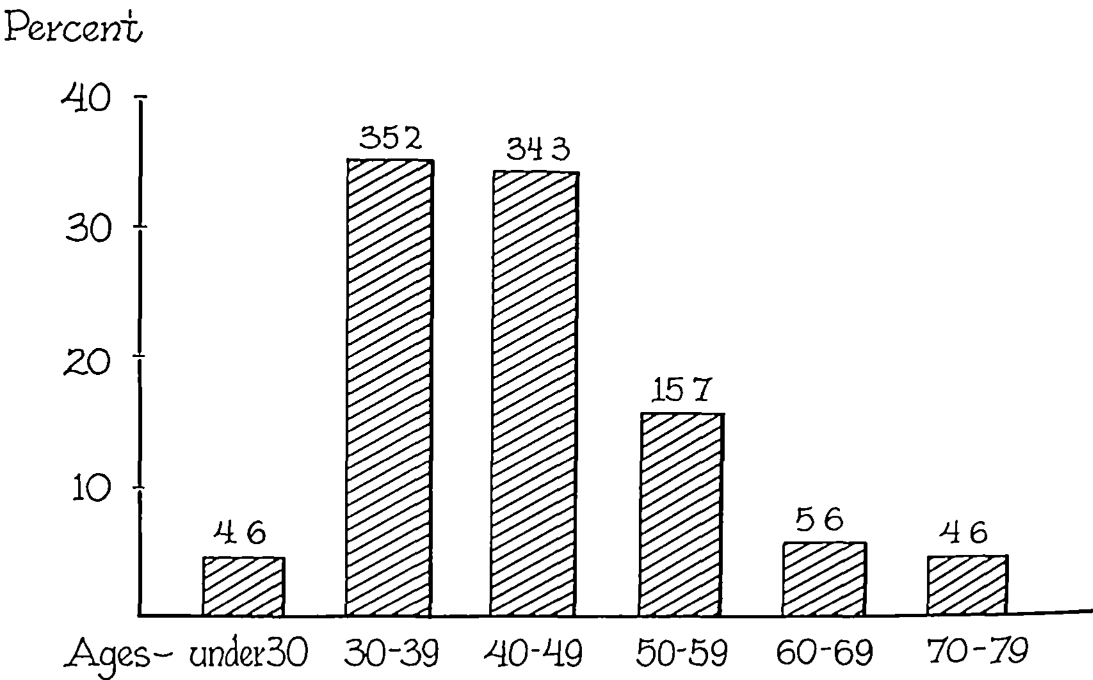
Clinical Features

Nipple Discharge A spontaneous nipple discharge is the most frequent symptom of intraductal papilloma. It occurred in 72 per cent of our series of patients with intraductal papilloma, and was more frequent, as Table 22 indicates, in the central than in the peripherally situated lesions The discharge was serous in 23 of the 78 patients and bloody in the remaining 55 In most patients it was

disease entity These lesions are one of the manifestations of cystic disease They are small multiple papillary projections, with or without fibrous cores, which project into the ducts and small cysts They are always multiple, often involve the ducts in many areas of the breast, and do not have a predilection for any special portion of it These microscopic papillomas rarely produce nipple dis-

Table 21. Intraductal Papilloma of the Female Mammary Gland
(Presbyterian Hospital 1916–1941 inclusive)

Total case records	367
Insufficient data for tabulation	14
Total benign papillary lesions	353
1 Microscopical papillomas	243
2 Gross intraductal papillomas	110
a Gross intraductal papillomas with unrelated carcinoma (not papillary)	2
b Gross intraductal papilloma for analysis	108



Percentage distribution of ages in 108 patients with gross intraductal papilloma
Chart 7

charge They are described in the literature as papillary hyperplasia, diffuse papillomatosis, cystiferous proliferation, etc We have data concerning 243 of these microscopic papillary lesions Since I have already dealt with cystic mastitis in Chapter 7, I will not discuss them further

The second group of benign papillary lesions, the grossly visible intraductal papillomas, are the tumors with which I am concerned in the present chapter This kind of papilloma usually forms a small but grossly visible tumor projecting into the lumen of the dilated terminal portion of a duct in the subareolar region Infrequently there are papillomas in several adjacent ducts The disease tends to be localized to the larger ducts in the central area of the breast We had records of 110 such benign intraductal papillomas in our study

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noted only intermittently, as evidenced by an occasional yellowish or brown stain on the brassiere or nightgown Long intervals would go by without any discharge in some patients In other patients the discharge was more consistent and abundant, slight pressure on the breast being sufficient to produce a flow of several drops of serum or blood

In a few patients there was a relationship between tumor formation and the discharge A tumor would slowly develop over a period during which there would be no nipple discharge A profuse discharge would then occur and the tumor would disappear as the distended duct or cyst emptied This cycle would be repeated over and over again

In an effort to determine why some papillomas cause a discharge from the nipple and others do not, all the microscopic sections were reviewed with this

Table 22 The Site in the Breast and the Frequency of Nipple Discharge in 108 Cases of Intraductal Papilloma

(Presbyterian Hospital—1916–1941)

Site in the breast	Number of cases	Per cent of total number of cases	Number cases with nipple discharge	Per cent with nipple discharge
Central	81	75	70	86 4
Peripheral	27	25	8	29 6
All sites	108	100	78	72 1

question in mind We found that the more solid glandular type of papillary disease in which a discharge is less frequent was more commonly located in the periphery of the breast This type of papillary proliferation also predominated in those centrally located lesions which did not show discharge from the nipple The highly papillary growths with multiple long dendritic processes which could readily be broken by the slightest trauma were found more commonly in the central portion of the breast This type of lesion was usually accompanied by a discharge

The location on the surface of the nipple of the duct from which the discharge escapes is an important indication of the radial situation of the papilloma in the breast Approximately 20 ducts open into the nipple surface, and the arrangement of these orifices has a close relationship to the radial course of ducts out into the breast For example, when a discharge is noted from a duct orifice at 9 o'clock on the nipple surface, the lesion, be it an intraductal papilloma or some other disease, will almost always be found in the corresponding 9 o'clock radius of the breast

In patients with a nipple discharge in whom no tumor can be found, palpation of the circumareolar region will often reveal a pressure point over some radius of its circumference Gentle pressure over this point produces a discharge from a duct orifice situated in a corresponding radius in the nipple surface Figure 168 shows this maneuver producing a drop of discharge from the nipple Moistening the nipple surface will sometimes assist in eliciting the discharge In this manner the site of the papilloma can often be localized

Tumor. Although the nipple discharge is usually the symptom that brings the

patient to the physician a tumor can be found by careful palpation in a considerable proportion of these patients I found a tumor in 19 of my 44 private patients with proved intraductal papilloma whom I treated between 1943 and 1954 It was sometimes felt indistinctly only as a linear thickening radiating out from beneath the edge of the areola or adjacent to it In our older Presbyterian Hospital series of cases a tumor was recorded as being present in almost all of the patients This fact indicates merely that in years gone by only the patients with a nipple discharge who had a palpable tumor were operated upon Today we often diagnose and correctly localize and excise intraductal papillomas that are not palpable

The 108 intraductal papillomas in our Presbyterian Hospital series of cases ranged in size from 0 3 cm to 10 5 cm the great majority being only 3 or 4 mm



Fig. 168 Expression of a drop of discharge from the nipple in a patient with intraductal papilloma by gentle pressure over site of papilloma in subareolar region.

in diameter and extending along the duct in which they arose for 1 or 2 cm In some of the cases the operator found a small, rounded, cystic structure containing bloody fluid and papilloma but failed to trace the duct extending from it to the base of the nipple

A special and infrequent form of intraductal papilloma that grows within the ducts of the nipple itself may be palpable as a small tumor within *the substance* of the nipple It may also grow out onto the surface of the nipple through the orifices of the nipple ducts and present on the nipple surface as a granulating lesion (Fig 169)

Retraction Signs Intraductal papillomas do not ordinarily produce retraction but occasionally skin dimpling, retraction of the nipple or distortion of the contour of the breast develops A good example of retraction was seen in the case of Mrs E. F whose history can be summarized as follows

noted only intermittently, as evidenced by an occasional yellowish or brown stain on the brassiere or nightgown Long intervals would go by without any discharge in some patients In other patients the discharge was more consistent and abundant, slight pressure on the breast being sufficient to produce a flow of several drops of serum or blood

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Tumor. Although the nipple discharge is usually the symptom that brings the

She was a 72 year old housewife who came to the hospital complaining of a bloody discharge from the left nipple which she had noted for the previous four months. The discharge consisted of a drop of very black blood noted every other day She went to her local physician who discovered a tumor in the breast, and referred her to the hospital.

Examination showed a firm 3 cm tumor lying beneath the edge of the areola of the left breast in the radius of 4 o clock The mass was relatively fixed in the surrounding breast tissue and there was marked dimpling of the overlying skin When the arms were raised, a deep notch became evident in the contour of the breast at the site of the tumor as shown in Figure 170 The breast and the tumor within it were freely movable over the chest wall

The surgeon mistakenly chose to do a radical mastectomy without frozen section Pathological examination of the breast showed that the tumor mass consisted of an intraductal papilloma solidly filling a cystic structure On microscopical examination the lesion proved to be a benign intraductal papilloma.

Pain Pain was noted as a symptom in only two of our 108 patients with intraductal papilloma

Table 23. Duration of Symptoms in 108 Patients with Intraductal Papilloma
(Presbyterian Hospital)

Duration	Number of Patients
3 months or under	37
4–6 months	18
7–12 months	15
2–3 years	10
4–5 years	10
6–10 years	8
Over 10 years	6
Not reported	4
	108

Signs of Inflammation. In one of our patients the clinical picture suggested an abscess The patient, a woman of 41 years who had not been pregnant for some years, developed swelling and tenderness of the left breast, accompanied by throbbing pain and the escape of a few drops of blood from the nipple A week later when she came into the hospital, there was a 4 cm indurated area in the outer middle section of the breast The skin over the outer half of the breast was reddened and abnormally warm Pressure upon the area of induration produced a flow of "dark reddish pus" from the nipple Culture of this material showed hemolytic *Staphylococcus aureus*

The lesion was excised and proved to be a small intraductal papilloma filling a distended duct, accompanied by acute inflammation in the surrounding breast tissue

Duration of Symptoms One of the clinical features of intraductal papilloma which weighs strongly in favor of the benign nature of the lesion is its long duration In the Presbyterian Hospital series of 108 cases the duration of symptoms was recorded in 104 (Table 23) In 14 the symptoms had been present for more than 5 years.



Fig 169 Intraductal papilloma presenting from surface of nipple



Fig 170 Retraction due to intraductal papilloma, evidenced as a notch in the contour of the lower edge of the breast

in Figure 172. Multiple benign papillomas arising separately in several ducts are sometimes found but they are uncommon

Microscopically intraductal papillomas are simply proliferations of duct epithelium which project outward into a dilated lumen from one or more focal points The proliferated epithelial cells are supported upon vascular stalks which may be thin and delicate (Fig 173) or broad and heavy (Fig 174) The prolifera tions may be obviously papillary or so completely anastomosing as to seem to form gland like spaces The structure depends upon the relative quantities of their component elements, together with the presence or absence of fresh or old blood necrosis, and fibrosis If they have suffered from repeated trauma, cica

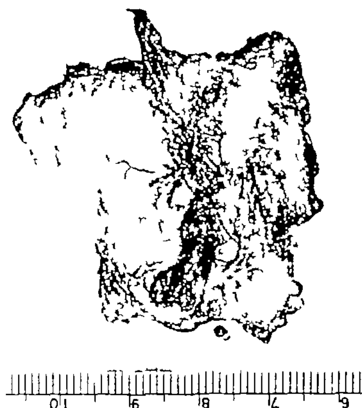


Fig 171 Gross appearance of intraductal papilloma lying in duct which has been opened. The proximal end of the duct, severed at the base of the nipple, projects from the top of the specimen

trices can form not only in the papillary projections but also in the wall of the dilated duct Such scars may include gland like tubes which can create a false impression of infiltrative growth (Fig 175) Another example of this process of fibrosis is shown in the low power photograph (Fig 176) of a papilloma that developed near the orifice of a nipple duct Here the original duct wall has almost disappeared, leaving the epithelial proliferations in a mass of scar tissue suggest ing the infiltrative growth of cancer This type of diffuse papilloma of the nipple has been well described by Jones, who has called it florid papillomatosis" of the nipple

The criteria which enable one to differentiate between benign and malignant, not only in this type of papilloma but also where the growth is wholly enclosed

A typical case history of an intraductal papilloma of long duration was that of S K , a housewife 38 years old Seventeen years previously, following weaning her first child, she had developed a discharge from the left nipple It consisted of a few drops of a brownish fluid which she noted only at intervals of from one to three months She learned that by squeezing the breast she could express a small quantity of the discharge This seemed to relieve her of a feeling of discomfort in the breast which she had from time to time During two subsequent pregnancies, twelve and eight years previously, the discharge had disappeared, and did not reappear until after the babies were weaned

Two years previously she had noted a small lump beneath the areola of the left breast This seemed to decrease somewhat in size when she squeezed her breast to express the discharge Examination showed a freely movable 2 5 cm tumor beneath the areola There were no retraction signs

At operation a thin-walled cystic structure filled with brown fluid and containing a papilloma growing from a broad base was found The lesion was excised locally, together with a small amount of adjacent breast tissue Twelve years later there had been no recurrence of either tumor or discharge

In other patients of ours with a serosanguineous nipple discharge who went through pregnancy, the discharge did not disappear during pregnancy or lactation, but stained the milk with blood and led to abandonment of nursing

Some patients noted that their nipple discharge was increased with the onset of menstruation, others reported no change during the menstrual cycle

Long intervals of freedom from the discharge were not uncommon, as in the case of A L , a nursemaid aged 62

She had first noted a serosanguineous nipple discharge ten years previously After a few weeks the discharge ceased and never reappeared Five years previously she had first discovered a tumor beneath the nipple This had not changed in size, but it had recently become tender

Examination showed a firm 3 x 3 cm mass beneath the areola of the right breast The mass was attached to the skin of the overlying areola, and to the nipple, which was somewhat flattened At operation the tumor was found to be a cyst containing brownish fluid and partly filled by a papilloma The cyst was excised The patient had had no recurrence when last seen eleven years later

Pathology

Intraductal papillomas are often so small and elusive that a precise technique is required to find and demonstrate them grossly When the offending duct has been identified and severed at the base of the nipple, and the mass of breast tissue around its peripheral course has been excised, the specimen should be laid out flat and the duct slit open with fine forceps and scissors As the duct and its branches are opened, extending peripherally, the papilloma will be found filling and distending it It is yellowish or hemorrhagic, and so soft and friable that it can easily be torn loose from the duct wall Figure 171 shows one of these papillomas which measured 2 cm in length The papilloma is usually attached only by a narrow pedicle, but may extend and lie free within the duct lumen for a distance of several centimeters It sometimes extends in this manner into the branches of the duct in which it arose The great majority of the benign papillomas are single lesions and are situated in a major collecting duct within 6 or 8 cm of its termination in the nipple When intraductal papillomas grow to a large size they form a friable, soft, hemorrhagic mass within a cystic cavity, as shown

in Figure 172. Multiple benign papillomas arising separately in several ducts are sometimes found but they are uncommon

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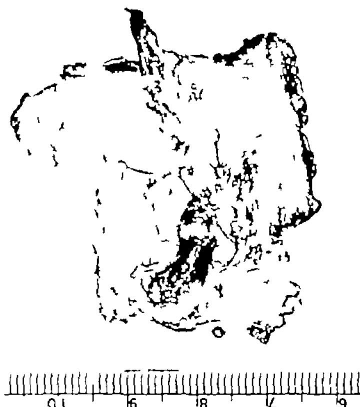


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within an intact duct wall, are to be found for the most part in the tumor cells themselves In benign growths the cells will resemble the cells of normal duct epithelium, whether of the usual type or of the so-called apocrine type, with small nuclei and large acidophilic granular cytoplasms It must be remembered, however, that normal duct cells vary considerably Not only are they capable of enlargement when engaged in secretory activity, but they can act as phagocytes and undergo degenerative changes with swelling and fatty infiltration In order to judge whether or not such abnormal appearing cells are cancerous, one must be familiar with these various changes which can take place in non-cancerous



Fig 172 Gross appearance of intraductal papilloma forming a soft, friable, hemorrhagic mass within a cyst

cells In doubtful cases, the decision generally rests upon the nuclei, if they have the appearance of anaplasia with hyperchromatism, accentuation of the chromatin network, or large nucleoli, and particularly if there are more than rare, widely separated mitoses, the lesion must be considered cancer If, in doubtful cases, there are small microscopic areas of cells which one might be tempted to consider suspicious of malignancy within an otherwise benign papillary tumor, we have classified them as benign Our experience has shown that the technique I have described for the local excision of benign papillomas will also cure papillomas showing this type of epithelial proliferation

The question of whether or not benign intraductal papillomas transform into papillary carcinomas is of course an important aspect of the argument regarding

Fig 173 Intraductal papilloma composed of delicate papillae



Fig 174 Intraductal papilloma with broad stalks

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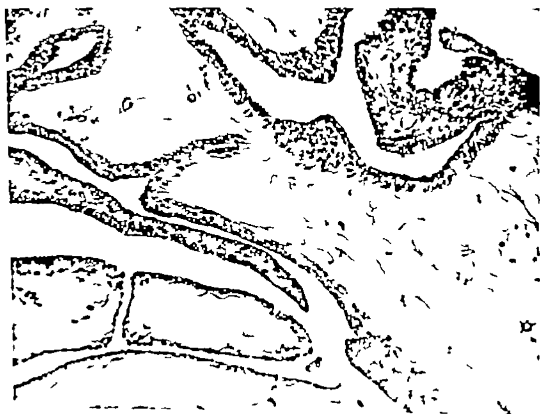


Fig 174 Intraductal papilloma with broad stalks.



Fig 175 Fibrosed intraductal papilloma giving the impression of infiltrative growth

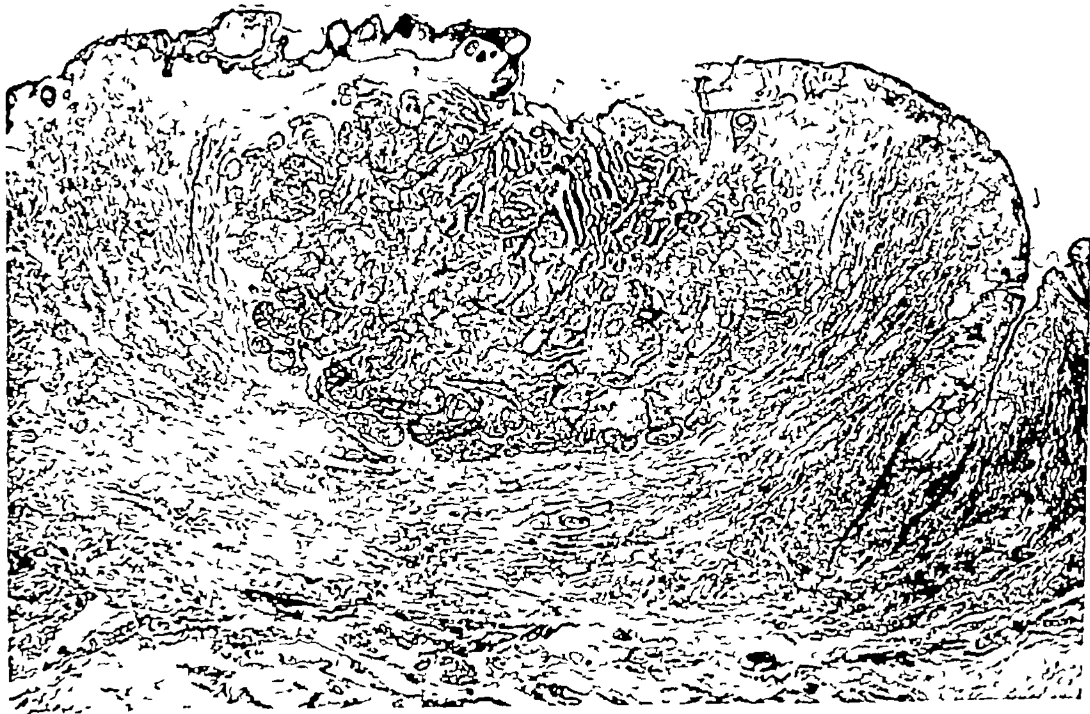


Fig 176 Intraductal papilloma growing within nipple

their treatment. I will deal with the question fully in Chapter 22 when I discuss papillary carcinoma, but I can state here that it is our belief that with rare exceptions intraductal papillomas do not become malignant, and should not be regarded as precancerous

Differential Diagnosis

There are several lesions which occur in the breast, in addition to intraductal papilloma which produce a nipple discharge Their variety is indicated in Table 24 which lists 118 private patients with a spontaneous nipple discharge whom I

Table 24. Nature of Disease in 118 Personal Patients with Spontaneous *Nipple Discharge (1943–1954)*
(Presbyterian Hospital)

Disease	With localizing signs	Without localizing signs
Intraductal papilloma	44	
Carcinoma	19	2
Cystic disease	5	
Adenosis	1	
Ectasia	3	
Infection	2	
Prolonged lactation (bilateral milky discharge)	0	1
Bleeding tendency (bilateral bloody discharge)	0	1
Pregnancy (bilateral bloody discharge)	0	2
Not operated (followed 3 to 7 years)	0	10
Not operated (no follow-up)	12	16
Total	86	32

studied in the period of 1943 to 1954 In 80 of them I was able to prove the nature of the lesion

It will be seen that in the majority of the patients in whom the cause of the discharge was identified it was an intraductal papilloma Carcinoma was the next most frequent lesion to produce nipple discharge Those carcinomas which produced a nipple discharge were almost all of the papillary type

In rare instances gross intraductal papilloma and carcinoma are found coexisting in the same breast and appear to be of independent origin The papilloma produces a nipple discharge and the carcinoma is silent There were two such cases in our Presbyterian Hospital series of gross intraductal papilloma Smaller papillomas found only microscopically may also produce a nipple discharge in the same breast in which carcinoma develops as exemplified by the following case history

Mrs J K a housewife aged 59 was admitted to Presbyterian Hospital with the history that for the past thirty years she had had intermittent spontaneous discharge from the left nipple In the beginning the discharge was usually bloody but as the years went by it changed to a yellowish color It was never profuse, only a few drops being noted at night Usually the patient would have a feeling of discomfort in the breast for a few days then the discharge would appear and the discomfort would be relieved She had recently noticed an indentation on the lateral aspect of the breast

All the classical signs of mammary carcinoma in the left breast were present The breast as a whole was contracted and slightly elevated The nipple was retracted Above and to the outer side of it there was a poorly delimited, hard tumor measuring about 4 cm in diameter

There was marked retraction of the skin over the tumor No enlarged axillary lymph nodes were palpated

Radical mastectomy was carried out The carcinoma that was found at the site of the tumor in the breast was of no special microscopical type It had metastasized to two of eight axillary lymph nodes



Fig 177 Intraductal papilloma coincidental with carcinoma of the breast

In one of the large ducts at the base of the nipple, a region to which the carcinoma had not penetrated, there was an entirely benign intraductal papilloma, shown in Figure 177 This benign papilloma was no doubt the cause of 30 years of nipple discharge, and I assume had no relationship to the carcinoma

Cystic disease, adenosis, duct ectasia, and some forms of infection in the breast, all occasionally give rise to a nipple discharge

An infrequent form of nipple discharge is a bilateral and bloody discharge not due to disease but to hyperemia or to a bleeding tendency During pregnancy the growth stimulation to the mammary epithelium is so great that in rare cases there is a slight bilateral bloody nipple discharge There were 2 such cases in my personal (1943–1954) series of 118 patients with a nipple discharge The following is a typical case history

Mrs J P, aged 35, was referred to me with the story that in the third month of her first pregnancy, which had terminated successfully two months previously, she had

noted, on one occasion only a slight amount of bright red blood from each nipple. She went to her obstetrician who in examining her breasts, squeezed her nipples and obtained a small amount of bloody discharge. He was alarmed and asked her to return repeatedly for examination, on each occasion expressing a slight amount of bloody discharge. She never again, after the first episode, had spontaneous nipple discharge.

After delivery her obstetrician forbade her to nurse. He continued to express a discharge from her nipples when he examined her but after her delivery it was never again bloody only whitish. He told her however that she would have to have biopsy of both breasts because of the discharge, but not being able to localize any lesion he finally referred her to me.

Her breasts were both normal to palpation. I could find no tumor and of course I did not attempt to express any discharge from her nipples because I know that a discharge that has to be elicited, and that does not occur spontaneously is not indicative of disease I reassured her and her doctor that the bloody discharge during her pregnancy was a physiological phenomenon.

As Table 24 indicates, there remained in my series of 118 private patients with nipple discharge a substantial number whom I did not succeed in getting back and localizing and proving the nature of the disease I fully realize as I have already emphasized in Chapter 5 that the only safe rule is to regard spontaneous nipple discharge as a sign of disease and urge surgical investigation Yet this is not always easily accomplished Patients make light of such a small thing as an occasional slight nipple discharge and the surgeon himself hesitates to explore a breast in which he cannot localize the lesion In my series of 118 patients there were 32 in whom there were no localizing signs and these patients made up most of the group who were not operated upon

Localizing signs of intraductal papilloma are in the order of their importance, a tumor a pressure point that produces the discharge and finally the radial situation of the orifice of the offending duct on the nipple surface. When all these localizing signs are lacking the only safe procedure is to re-examine the patient at weekly intervals for a month meticulously searching for a localizing sign that will indicate in what sector the lesion is situated If localizing signs are not found surgical exploration should nevertheless be carried out Unless this practice is followed carcinoma will in rare instances be missed There is no other reliable method of identifying the particular lesion which is producing the nipple discharge As I have pointed out in Chapter 5 the methods of injecting the mammary duct do not give definitive information

Treatment

The disagreement regarding the correct treatment of intraductal papilloma and the mistakes that are made in treatment are chiefly due to a lack of knowledge of the pathology of the disease on the part of the surgeons Many are not familiar enough with the gross appearance of a duct containing a papilloma to be able to find it at operation The dissection must, moreover be a meticulous one in which bleeding is carefully controlled or it will not be possible to see the lesion Handicapped by these difficulties the average surgeon who attempts local excision of an intraductal papilloma has been content merely to excise blindly the area of breast tissue which he presumes contains the lesion without dissecting it out and identifying it When local excision is done in this manner it is not

surprising that recurrence occasionally develops from papilloma left behind Such recurrences are mistakenly interpreted as the malignant transformation of the papilloma, and needless mastectomy is performed

Another cause for confusion regarding the treatment of intraductal papilloma is the difficulty that some pathologists have in distinguishing microscopically benign papilloma from papillary carcinoma The less courageous pathologists tend to classify a good many entirely benign lesions as malignant I know that this distinction is not an easy one, but I believe that with adequate experience it can be made with certainty in almost every case When the pathologist is in doubt, he had better delay and seek more expert diagnostic help before deciding that the lesion is malignant He should remember that papillary carcinomas are rare, and even if the lesion in question proves to be a carcinoma, a reasonable delay will not impair the chance of cure by radical surgery, because the growth vigor of papillary carcinoma, like the other well differentiated carcinomas of the breast, is decidedly less than that of the ordinary breast carcinoma

Experience has convinced me that intraductal papillomas can be accurately diagnosed, and local excision is all that is required Mastectomy is unnecessary This belief rests upon my own personal experience, as well as upon the follow-up study of our Presbyterian Hospital cases that Dr Stout and I made It is worth while referring to this study again

The treatment of the 108 patients with benign intraductal papilloma in our series varied considerably, depending upon the surgeon in charge of the patient The period covered by our study extended over twenty-six years and almost all of the surgeons on the hospital staff were concerned Some of our surgeons persisted in believing that intraductal papilloma is a potentially malignant lesion and therefore inclined to carry out radical therapy Fortunately for the purposes of our study, the majority were convinced of the benignancy of this lesion and were content to do conservative local excision Table 25 shows the type of treatment in our series of cases Thirty-two of our patients had either radical or simple mastectomy, while in 76 only local excision of the lesion was performed

Table 25 The Treatment of Intraductal Papilloma According to the Site of the Lesion in the Breast

(Presbyterian Hospital 1916–1941)

Type of treatment	Central site	Peripheral site	Total all sites	Per cent of total
Radical mastectomy	9	3	12	11
Simple mastectomy	16	4	20	18 5
Local excision	56	20	76	70 5
Total treated	81	27	108	100

In the 12 patients in whom radical mastectomy was carried out, the reason for this needlessly radical therapy was in every instance mistaken diagnosis of carcinoma In 3 of these cases the surgeon was responsible for the error In 2 of these cases he proceeded without a biopsy, while in a third case he went ahead on the basis of an incorrect aspiration biopsy diagnosis of carcinoma made in

another hospital In the remaining 9 cases the pathologist was responsible because he made a mistaken microscopical diagnosis of carcinoma

In 4 of these cases this mistake was made with adequate paraffin sections available for study but in the remaining 5 cases the pathologist based his opinion solely upon frozen sections During the past ten years we have not made a mistake of this kind because we have learned in questionable cases not to rely upon frozen sections in distinguishing benign from malignant papillary tumors of the breast Frozen sections are not adequate for this difficult microscopical diagnosis During the last decade it has been our practice *to advise biopsy only* in cases in which the surgeon when exploring a supposed papilloma of the breast for which he intends to do a simple local excision finds features which suggest the possibility of the lesion being malignant Following removal of a satisfactory piece of the lesion the wound is closed and we wait for paraffin sections upon which to base our diagnosis If the lesion proves to be benign it is locally excised at a second operation If it is malignant, radical mastectomy is done. We believe that the disadvantage of having to delay and carry out our definitive treatment at a second stage is more than compensated for by the avoidance of the risk of subjecting the patient to an unnecessary mastectomy for a benign papilloma

In 20 patients simple mastectomy was done The reasons for this choice were not always apparent in the case records In some instances the surgeon s lack of confidence in his pathologist s ability to distinguish benign papillary disease from carcinoma in the breast was the basic reason This was the obvious explanation for the 5 cases in which biopsy and frozen section were done and the pathologist made a diagnosis of benign papilloma, yet the surgeon proceeded to remove the breast In one other case the surgeon was wrongly told by the pathologist that the frozen section showed a precancerous lesion he of course did a mastectomy In four additional cases the surgeon had not localized the papilloma by his clinical examination and he failed to find it at operation He resolved this dilemma by performing a simple mastectomy and excused his drastic therapy on the ground that it was a prophylactic measure against the development of carcinoma.

In the 76 patients in whom local excision was the method of treatment the thoroughness of the excision varied with the operator s understanding of the pathology of intraductal papilloma In most of the cases the surgeon simply cut down upon the tumor and excised it, and did not attempt to identify it and dissect out the duct or ducts in which the papilloma arose Often he did not recognize that he was dealing with an intraductal papilloma until the pathologist made the diagnosis for him

In a limited number of cases surgeons with a better knowledge of the disease made a correct clinical diagnosis of benign papilloma, determined its site and excised it locally This is the ideal method of treatment

Table 26 shows the follow up of 76 patients in the Presbyterian Hospital series in whom local excision of an intraductal papilloma was performed It was possible to follow 72 or 94 7 per cent of the 76 patients Only 4 were lost after all means of contact were exhausted

Three of the 72 patients died of intercurrent disease before five years had elapsed—one month 16 months and 28 months following operation Three other patients developed recurrences 2 under five years and 1 more than five years

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years later in 1942, when examination showed a 4 cm mass beneath the scar of the previous operation Biopsy then showed that the tumor was still a benign intraductal papilloma, and another local excision was done She was last seen five and one-half years later without evidence of tumor in either breast.

Case 4 Mrs. M R aged 30 came to the Presbyterian Hospital in 1938 She had noticed a small crusted area on her left nipple for over a year There was a small amount of yellowish discharge from it from time to time Palpation of the breast failed to reveal any tumor Close inspection of the nipple showed that the orifice of one of the nipple ducts was dilated and that projecting from it was a soft reddish papillary mass about 3 mm in diameter This was assumed to be an intraductal papilloma of the terminal portion of the duct At operation a sector of the nipple, including the diseased duct, was excised The excision was carried to the base of the nipple and a little way down into the breast Microscopical examination showed that the lesion was indeed an intraductal papilloma. It projected from the orifice of the duct and extended down along its branches to the base of the specimen. It was not certain from the study of the microscopical sections that the papilloma had been excised in its entirety

The follow-up of this patient showed, however that the excision was adequate, for she has had no further trouble with the left breast But nine years later in 1947 she entered another hospital for bleeding from the right nipple A local excision of the subareolar area was done and benign intraductal papilloma found

This case is therefore an example of the development of a new papilloma in the contralateral breast.

Case 5 Mrs. H. H a housewife aged 38 came to the Presbyterian Hospital in 1939 because of a tumor in her left breast which she had noticed fourteen months previously There had been no nipple discharge. Examination showed a firm but circumscribed 3 cm. tumor just beyond the mesial edge of the left areola At operation the tumor was found to be cystic and filled with friable papillary tissue. It was excised, and microscopical examination confirmed the diagnosis of benign intraductal papilloma

In 1947 the patient noted a new tumor in the left breast. It lay in a different site from her original tumor being at the lateral rather than the medial edge of the areola It was 3 cm in diameter At operation the lesion was found to be a group of small cysts containing papillary tissue. The dilated ducts containing papilloma were traced to the base of the nipple and resected together with the cystic mass. The lesion was, like the original tumor eight years previously a benign intraductal papilloma When the patient was last seen seven years later there had been no further recurrence

We assume that this case illustrates the development of a new intraductal papilloma in another sector of a breast previously involved by the same type of lesion.

The follow up in a considerable number of patients in this series was a long one In a total of 31 patients in whom local excision only was done, the total observation period including the length of time symptoms had been present before treatment and the length of the follow up after operation ranged from 10 to 29 years The fact that carcinoma did not appear in any of these patients during this long period of time is good evidence that their lesions were indeed benign

My method of dealing with a breast lesion that has the clinical characteristics of an intraductal papilloma includes first of all a frank explanation to the patient of the special difficulties of diagnosis and of the possibility of carcinoma In the operating room under general anesthesia, an incision through the skin is made about halfway around the circumference of the areola (Fig 178*A*) The incision is centered at the radius in which the lesion is presumably situated as indicated by the position of the tumor or by other localizing signs. The incision is placed precisely at the areolar edge This minimizes the scar The incision

Table 26. Follow-up of 76 Patients with Intraductal Papilloma Treated by Local Excision
(Presbyterian Hospital 1916–1941)

Site in the breast	Total cases treated by local excision	Lost track of	Died of intercurrent disease before 5 years	Cured		Recurrence of papilloma		Developed carcinoma	Total cases followed	Per cent follow-up
				5 Yr +	10 Yr +	Under 5 yrs	After 5 yrs			
Central	56	3	3	28	20	2	0	0	53	94 6
Peripheral	20	1	0	12	7	0	1	0	19	95 0
All sites	76	4	3	40	27	2	1	0	72	94 7

after the original operation In 2 other patients who were followed for five or more years, 1 developed a new papilloma in the opposite breast after nine years, and the other a new papilloma in the opposite quadrant of the same breast after eight years *No patient in this series developed carcinoma*

It is instructive to summarize the histories of the three patients who developed recurrence after local excision, and the 2 patients who developed new papillomas elsewhere in their mammary tissue, because they illustrate the difficulties that surgeons and pathologists get into in dealing with intraductal papilloma, unless they know the disease well and can cooperate

Case 1 Mrs O R, was a 38 year old woman, first seen in 1930, complaining of a bloody discharge from the left nipple of seven years' duration She had had a lump in her breast for six weeks On examination she had a 4 x 5 cm mass at the areolar margin which was freely movable Local excision was attempted, but the surgeon failed to recognize that the lesion was a papilloma He cut directly down on the tumor and excised it without tracing the diseased duct to the nipple, or identifying its peripheral extension With this kind of limited excision it is very likely that part of the duct or ducts containing papilloma were left in situ Microscopically the original lesion was a benign intraductal papilloma

Approximately four years later there was a recurrence in the scar of the previous operation The new tumor was biopsied, a frozen section diagnosis of carcinoma made, and radical mastectomy carried out Fixed sections, however, proved the recurrent lesion to be identical with the original benign intraductal papilloma The mastectomy was clearly unnecessary

Case 2 Mrs D B was first seen in 1937, when she was 34 years of age She complained of a bloody discharge from the left nipple of three years' duration, a lump in the breast of one year's duration Examination revealed a 2 x 3 cm shotty mass at the upper inner areolar margin A partial mastectomy was done In this patient also, the tumor was cut down upon and broken into several pieces, and shelled out bluntly, without any attempt to trace the diseased duct, either centrally or peripherally Microscopically it was a benign intraductal papilloma

In 1941 there was a 0 5 cm recurrent tumor in the scar of the previous operation A second partial mastectomy was done At this time a pyramidal sector of breast tissue, including the diseased duct system centrally and peripherally and down to the pectoral fascia, was removed Five years later, she was free of disease in both breasts

Case 3. Mrs V H, aged 48, came to the Presbyterian Hospital in 1935 She complained of a lump in the right breast of three weeks' duration, without a history of nipple discharge There was a 2 x 2 5 cm mass in the upper outer quadrant of the right breast The tumor was cut down upon and found to be a cyst filled with friable hemorrhagic tissue, and crudely excised No attempt was made to trace the extent of duct involvement by the papilloma Recurrence in the scar was noticed approximately seven

excise a wedge shaped sector of mammary tissue surrounding the diseased duct To accomplish this the first step is to incise the breast tissue centrally to the diseased duct to form the central edge of the area of breast tissue to be excised (Fig 178*C*)

The next step is to elevate a flap of skin and subcutaneous tissue from the peripheral edge of the wound uncovering the sector of breast tissue to be excised This is done by retracting the peripheral edge of the wound with skin hooks and undercutting the skin for a distance of 5 or 6 cm (Fig 178*D*) This done, the skin hooks are exchanged for four small abdominal retractors exposing the area of breast tissue to be excised The size of the sector excised varies somewhat with the size of the breast but it is my practice to carry the excision about 5 cm out toward the periphery of the breast With the diseased duct at its center the cone of breast tissue to be removed is then elevated and excised beginning at its central edge and encircling it peripherally (Fig 178*E*) As the base of the cone of breast tissue is being cut across, great care is taken to keep the operative field dry so that if any ducts are seen to contain extensions of the papilloma as they are cut across a wider excision can be carried out When the specimen is out I ask the pathologist to open the duct that presumably contains the papilloma while I watch him I wish to make certain myself that I have found and removed the lesion producing the nipple discharge.

After careful hemostasis the wound is closed without drainage. The circum areolar incision if properly closed with subcuticular and skin sutures of silk leaves a scar which is almost invisible I dress the wound with gauze fluffs held in place by an Ace bandage to give gentle compression This is left undisturbed for a week when the sutures are removed. Some blood or serum not infrequently collects in these wounds, and requires aspiration when the wound is dressed This is preferable in my opinion to placing a drain in the wound

With this technique I have rarely failed to find and remove intraductal papillomas when they are the cause of nipple discharge Occasionally cystic disease or duct ectasia will be found, and of course excised When I encounter papillary proliferation in many ducts, and involving an extensive area of the breast I at once suspect that the lesion is a papillary carcinoma With this finding I do not proceed with either wide local excision or mastectomy Instead I remove a small biopsy from a representative portion of the lesion and close the wound As I have already pointed out, frozen section differentiation between the benign intraductal papilloma and intraductal carcinoma is too difficult to be reliable We depend only upon good paraffin sections In this manner we safely and surely identify benign papilloma and avoid needless sacrifice of the breast

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should not extend more than halfway around the areola, for fear of causing necrosis of the areolar flap

Traction of the areolar flap is made with four skin hooks of the type described in Chapter 6 I then dissect up the areolar flap to the base of the nipple and dissect out the ducts which radiate from it The dissection must be performed with delicacy, and meticulous hemostasis achieved with mosquito hemostats, otherwise the pathology will be obscured The duct containing the papilloma can usually be identified by its size and color It will be dilated to a diameter of something like 3 or 4 mm, and the serum or blood which it contains gives it a bluish

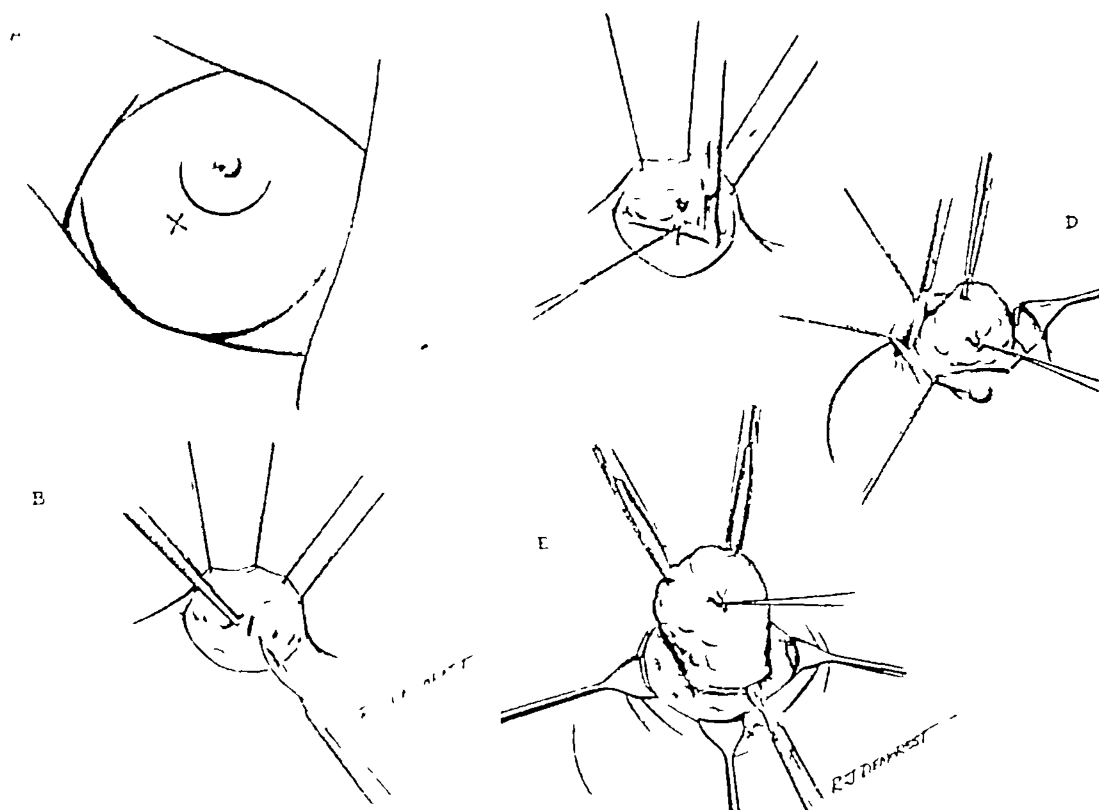


Fig 178 Method of excision of intraductal papilloma *A*, circumareolar incision, *X* marks the site of the papilloma *B*, dissection to the base of the nipple of the dilated duct containing the papilloma *C*, incision of the breast tissue central to the diseased duct *D*, dissecting up a peripheral flap of skin and subcutaneous tissue to uncover the area of breast tissue to be excised *E*, excision of the area of breast tissue containing the diseased duct

appearance (Fig 178*B*) Having identified and isolated it, I clamp it and cut across it at the base of the nipple Unless the involved duct is dissected out to the very base of the nipple, there is danger of not removing the papilloma in its entirety, for the branching processes commonly grow along the duct very close to the nipple base Occasionally several ducts are involved by the papillary proliferation, and then each one must be dissected out and severed at the base of the nipple When the diseased ducts are cut across, they will be recognized by their enlarged calibre and by the escape of the characteristic yellowish or bloody fluid I often cut across all of the ducts at the base of the nipple in making certain that I have found the duct containing the papilloma No harm results

Without further effort to trace the diseased duct out into the breast, I then

excise a wedge shaped sector of mammary tissue surrounding the diseased duct To accomplish this the first step is to incise the breast tissue centrally to the diseased duct to form the central edge of the area of breast tissue to be excised (Fig 178*C*)

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CHAPTER 14

NON-EPITHELIAL TUMORS OF THE BREAST

In grouping together in one chapter a dozen different types of neoplasms of the breast I have only the excuse that they are all non-epithelial in origin and that they are all infrequent A separate chapter for each would complicate unreason ably my plan for chapter division

I have included both benign and malignant non-epithelial tumors, grouped according to their histogenesis I do not pretend to present a complete catalogue of all the various types of non-epithelial tumors that may occur in the breast, but I will present examples seen in the laboratory of Surgical Pathology of the Col lege of Physicians and Surgeons during Dr Stout s forty odd years of direction

Fibrosarcoma

Fibrosarcoma is the most frequent type of malignant non-epithelial tumor developing from the soft tissues of the body There were 403 fibrosarcomas among the 1 349 malignant mesenchymal tumors studied by Dr Stout Yet fibrosarcoma is one of the rarest neoplasms of the breast.

Dr Stout separates fibrosarcomas in general into two classes, the well differen tiated tumors and the poorly differentiated ones The former often recur after the usual inadequate local excision, but they rarely metastasize and are rarely fatal The fibrosarcomas that arise in the skin, called *dermatofibrosarcoma pro-tuberans* or *dermatofibroma* belong to the well differentiated class They grow slowly and infiltrate the skin widely but have little tendency to penetrate deeply The poorly differentiated fibrosarcomas, in contrast, not only regularly recur locally after inadequate excision but they metastasize through the blood stream and are fatal in more than one half of the patients

At the Presbyterian Hospital we have had only one good example of each of these two classes of fibrosarcoma of the breast Abstracts of these two cases follow

Dermatofibrosarcoma of the Breast Mrs. M C. a 33 year old housewife, came to the Presbyterian Hospital complaining of a recurrent tumor of the left breast.

Four years previously she had first noted a tumor of the left breast. It was excised at another hospital and proved to be an adenofibroma, without any unusual features. A year later recurrence was noted in the operative scar

Examination on admission showed a 6 cm. scar following the skin lines, in the skin of the outer sector of the left breast It was situated between the radius of 3 and 5 o clock and 3 cm. out from the edge of the areola In the skin scar there were two firm nodules, measuring 1 5 and 1 cm. respectively in diameter These were elevated slightly

Fig 179 Well differentiated dermatofibrosarcoma beneath the skin of the breast

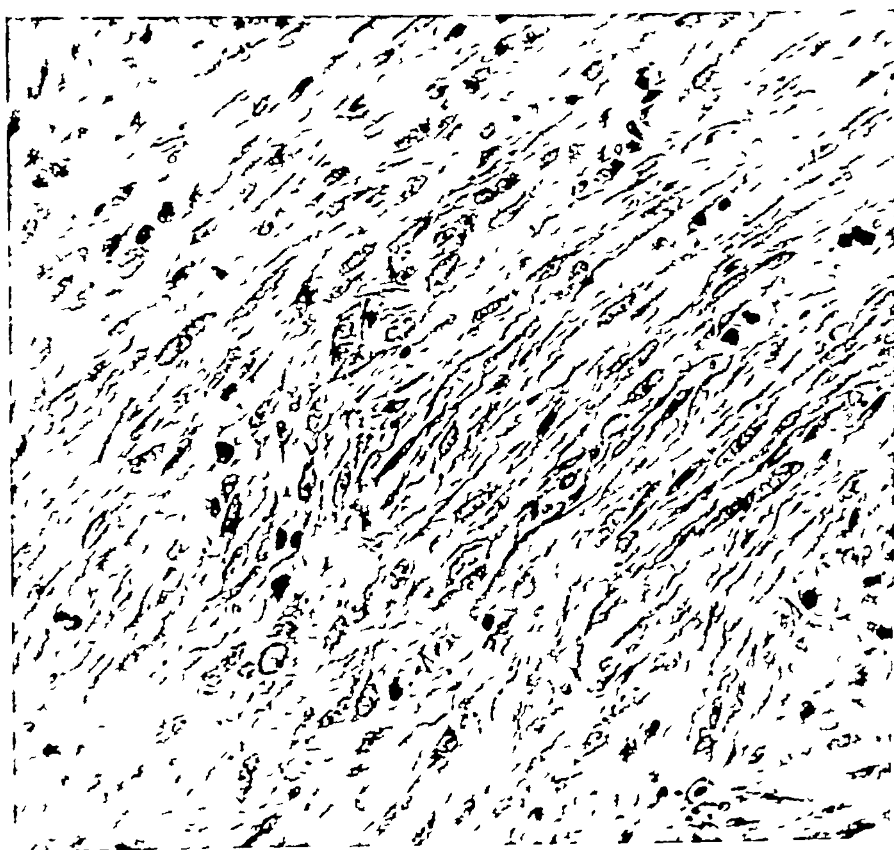


Fig 180 Fibrosarcoma of the breast
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above the skin surface and covered with intact thin somewhat reddened epithelium The underlying breast was normal to palpation.

I excised the scar with its nodules, including 1 5 cm of normal skin on each side of the nodules, together with some underlying breast tissue When the specimen was cut the nodules were seen to be sharply circumscribed, white and fibrous and limited to the skin and subcutaneous tissue. Microscopically they were well differentiated fibrosarcoma (Fig 179)

Three years later recurrence in the scar of my operation was noted This recurrence was in the form of a series of minute nodules along the scar line These slowly enlarged, and six years after my first operation I did another and more aggressive excision of the scar and tissues adjacent to it This time the line of excision was carried a distance of 5 cm on each side beyond the scar and 2 cm of the underlying subcutaneous fat and breast tissue included. The denuded lower half of the breast was skin-grafted Again microscopical examination showed a very superficial well differentiated fibrosarcoma. At the present writing two years after my second operation there has been no further recurrence.

Fibrosarcoma of the Breast Mrs. C M a 48 year old housewife was admitted to the Presbyterian Hospital complaining of a tumor of the breast that she had just noted five days previously

Examination revealed a hard rounded tumor in the right breast situated just caudad to the areola It measured about 5 cm in diameter It was movable within the breast tissue. The overlying skin was not involved There was no retraction.

At operation the tumor was excised locally together with a 2 or 3 cm margin of surrounding breast tissue No lymph node dissection was done

Grossly the tumor was well circumscribed and measured 3 5 cm in diameter Its cut surface was fibrous and trabeculated Microscopically it was a characteristic malig nant fibrosarcoma without any apparent relationship to the breast tissue except for invasion at the margins Its spindle-shaped cells varied considerably in size and shape, and showed an average of two mitoses per high power field (Fig 180) There were sev eral areas of typical osteoid in the tumor Dr Stout classified it as a poorly differen tiated malignant fibrosarcoma with osseous metaplasia

The patient had had no recurrence when she was last seen, eighteen years after her operation

Treatment of Fibrosarcoma The well differentiated fibrosarcomas of the breast require only local excision but this excision as illustrated by my failure to get the disease out in my first try in my patient should include the tissues at least several centimeters beyond the gross limits of the tumor

The undifferentiated fibrosarcomas should be attacked more vigorously removing a wider margin of grossly uninvolved tissue I see no reason however for removal of the entire breast Certainly there is no justification for an axillary dissection because fibrosarcomas do not, in general metastasize to the regional lymph nodes Distant metastases when they occur go through the blood stream

Radiotherapy should not be used for fibrosarcomas They are exceedingly radioresistant

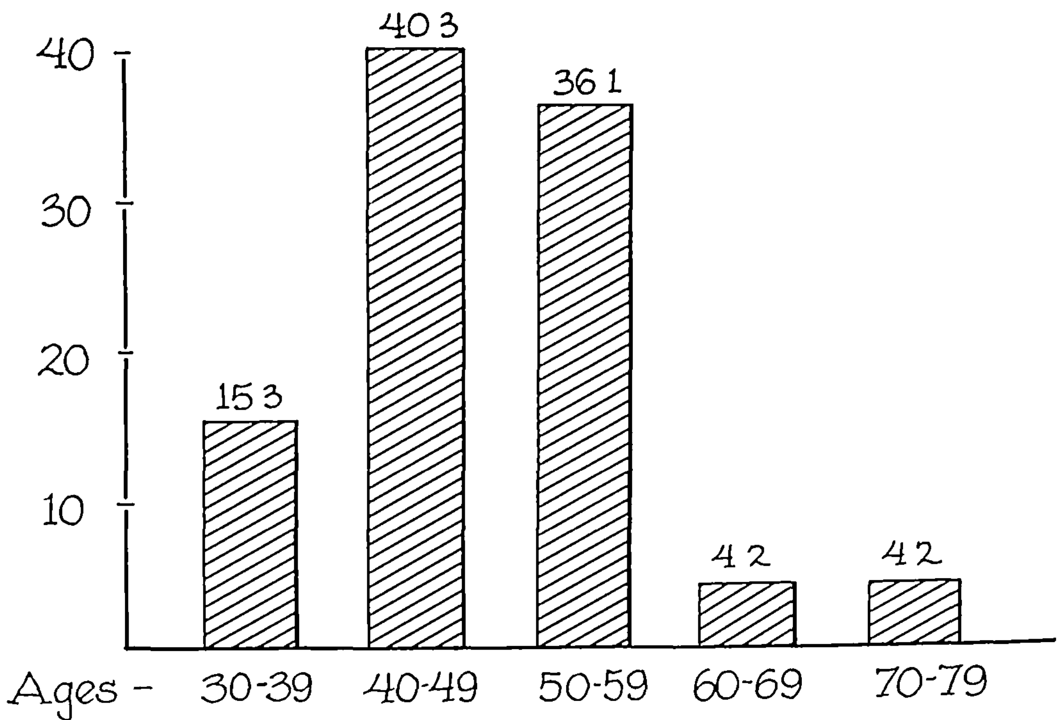
Lipoma

Since the lipoma is one of the commonest benign neoplasms and is found in all parts of the body it is not surprising that it is not rare in the breast. In our clinic we have seen two or three of these tumors yearly Over a twenty six year period (1927 to 1953) a total of 72 were recorded in our laboratory of surgical pathology

Lipomas develop in the breasts of older, rather than younger, women The mean age of our group of patients was 47 Their age distribution is shown in Chart 8

Breast lipomas are usually solitary lesions I have seen only one patient in whom the breast lipoma was associated with multiple subcutaneous lipomas in other parts of the body This was a woman who had multiple lipomas on the arms and trunk for many years when, at the age of 66, one developed in the lower inner sector of her breast

These tumors produce no symptoms They grow slowly Ten of our 72 patients had had their tumors for more than two years In three the duration was 15 years or more



Percentage distribution of ages in 72 patients with lipoma of the breast

Chart 8

With their long duration lipomas of the breast may grow to a large size In one quarter of our patients the tumor measured more than 5 cm in diameter, and eight of these tumors were 10 cm or more in diameter

Breast lipomas are soft, movable, and fairly well delimited, although their outline tends to be lost in the soft texture of the breast They do not, of course, produce retraction

The lesion that lipomas of the breast are most apt to be confused with clinically is cystosarcoma The latter tumor is apt to grow more rapidly, but this is a small point in differentiation

The gross pathological character of lipoma of the breast is so close to that of normal fat in a fatty breast that close inspection is sometimes necessary to identify

it The lipoma has of course a delicate capsule (Fig 181) and its color is usually slightly different from the normal fat of the breast being more yellow

Cystosarcoma sometimes has a pale yellowish color that suggests lipoma at first glance It is important to distinguish the two lesions and a frozen section should always be made if there is any doubt A lipoma may be shelled out, while cystosarcoma as I have already pointed out should be excised with a margin of the surrounding breast tissue

The following case history is typical of lipoma of the breast

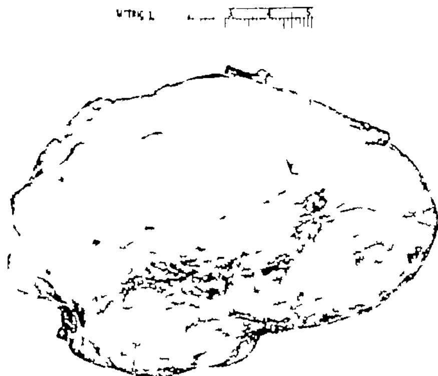


Fig 181 Gross appearance of lipoma of the breast.

Miss M W a 58 year old woman, came to the Presbyterian Hospital with the complaint that her breast tumor had reached a size that inconvenienced her She had had it for fifteen years, and it had slowly increased in size during the last few years. It was situated in the lower inner sector of the left breast and measured 10 cm. in diameter It was soft, well delimited and movable It was exposed and excised through an infra mammary incision, chosen because I was convinced it was benign and it proved to be a simple lipoma.

Adenolipoma

A special type of fatty tumor peculiar to the breast, has been called *adenolipoma* It is indeed a lipoma, but one in which fat is intermingled with epithelial lobules

Spalding published a good description of one of these tumors seen at Guy's Hospital At the Presbyterian Hospital we have studied eight adenolipomas during the 10 year period 1943–1953 Although this group is too small for the age distribution to be of any significance the patients were younger than the women with simple lipomas In several of the patients the tumors had been present a

number of years In size the tumors were not dissimilar from our series of simple lipomas

A rather striking example of adenolipoma in our group of cases follows

M L, an unmarried girl aged 18, was admitted to the Presbyterian Hospital complaining of a tumor of the right breast of six months' duration

The inner half of the right breast was distended by a soft, well circumscribed, movable tumor measuring 12 cm in diameter (Fig 182)

It was excised and found to be a typical encapsulated adenolipoma The gross appearance of its cut surface was characteristic of these tumors It showed yellowish fat with small brick red, slightly raised lobules of more firm epithelial tissue dispersed throughout

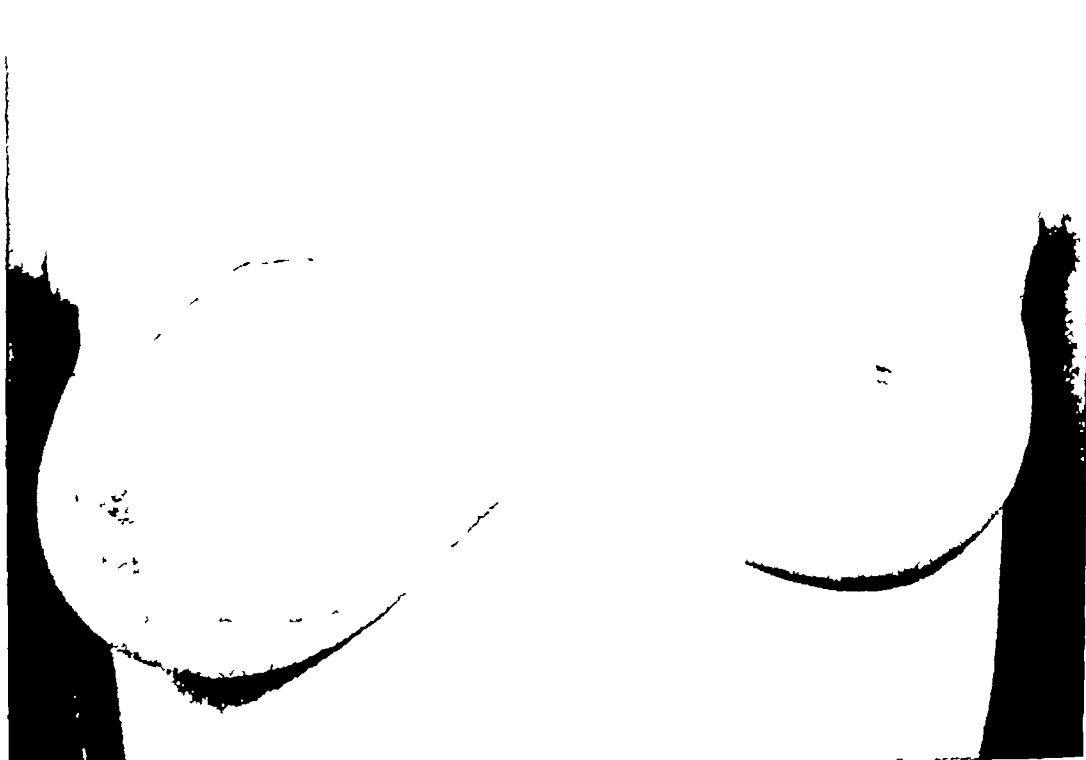


Fig 182 A large adenolipoma of the breast

The moot question regarding adenolipoma is whether the epithelial elements, as well as the fat, are neoplastic, or whether the neoplastic fat merely infiltrates the normal mammary epithelial elements The frequency with which lipomas diffusely infiltrate other tissues such as skeletal muscles is of course well known The fact that in adenolipomas the mammary acini are seen lying naked, so to speak, in immediate contact with the neoplastic fat, as shown in Figure 183, suggests that the second explanation is the best one

The tumors are, of course, entirely benign, and local excision suffices

Liposarcoma

Liposarcoma is, next to fibrosarcoma, the most frequent of the soft tissue sarcomas There were 262 liposarcomas among the 1,349 malignant mesen-

chymal tumors in Dr Stout s series Only 2 of these liposarcomas originated in the breast They were both of the undifferentiated variety and fully malignant. One of these tumors illustrated the tendency of liposarcomas to grow to an impressive size for it was 12 cm in diameter It was treated by simple mastec tomy which failed to check it the patient dying six months later

The other liposarcoma was described by Stout and Bernanke in a paper in which they also collected the previous case reports of breast liposarcoma A summary of this case follows

A married woman, age 43 noted a tumor in her left breast. Examination showed a freely movable 2.5 x 1 7 cm. tumor of the upper outer sector of the breast. It was not attached to the skin There were no enlarged axillary nodes.



Fig 183 The microscopical appearance of adenolipoma of the breast.

At operation the tumor was excised locally with a wide margin of surrounding breast tissue. Gross examination revealed that it was well circumscribed soft light brown in color and 1–2 cm. in diameter Microscopically it was a partially differentiated liposarcoma Figure 184 shows its myxoid stroma and bizarre giant cells. The infiltrating character of the tumor is shown in Figure 185 where it is seen infiltrating a mammary lobule The patient was well seven years later

Granular Cell Myoblastoma

Granular cell myoblastoma is an infrequent type of neoplasm first described by Abrikossoff in 1926 Although the lesion is most frequently seen in the tongue it may develop anywhere in the body In 1946 Stout and I described five granular cell myoblastomas that we had observed in the breast and referred to three other cases that had been recognized and reported by Abrikossoff by Meyer and by

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Gray and Gruenfeld Since our paper appeared Powell Simon and Crawford and DeBakey have described three additional breast myoblastomas and we have dealt with one more in the Presbyterian Hospital It was a 1 cm tumor overlying the second rib 5 cm from the sternal edge in a woman aged 40 It is of interest to add in regard to this patient that five years later she developed carcinoma of the lower outer sector of the same breast I assume that her carcinoma and myoblastoma were unrelated

The history of one of our cases might be taken as typical of this lesion

Mrs N B a Russian born Jewess, first came to the Presbyterian Hospital in 1928 when she was 47 years of age She was found to have hypertensive cardiovascular disease, and mild diabetes She failed to follow her diet and gained a good deal of weight as the years went by In 1935 she was put on insulin.

In February 1944 at the age of 63 she discovered a tumor in her left breast. It presented on the inferior aspect of the large dependent breast just cephalad to the infra mammary fold It was therefore, concealed when the patient sat erect and in this position the only evident abnormality was slight elevation of the breast. It was very evident with the patient in the supine position, however as a projecting tumor situated over the fifth interspace half way between the sternal edge and the nipple line. It was hard, and measured 4 cm in diameter The tumor and the breast tissue in which it lay were relatively fixed to the underlying chest wall. When the breast was pushed medially toward the tumor a definite dimple appeared in the skin over it No enlarged axillary nodes were detected

A presumptive diagnosis of carcinoma of the breast was made and all preparations completed for a radical mastectomy Fortunately a biopsy was done a small wedge being removed from the surface of the lesion for frozen section The only feature of the gross appearance that suggested something unusual was the fact that the cut surface of the tumor was whiter than most carcinomas (Fig 186) When the frozen section revealed that the lesion was a granular cell myoblastoma it was excised locally and the wound closed. Healing was uneventful There had been no recurrence when the patient was last seen ten years later

The tumor was made up of myoblasts with small oval nuclei and large finely granular cytoplasms (Fig 187) The cells lay in solid masses and strands, often in immediate contact with one another without any intervening collagenous reticulum The Scharlach R stain failed to show any lipoid in the cells. The edge of the lesion was sharply defined against the adjacent mammary tissue, but there was no true capsule.

The source of the muscle cells from which these myoblastomas arise in the breast is an intriguing, although perhaps a somewhat theoretical question Abrikossoff traced the origin of these tumors to striated muscle and the fact that their most common site is the muscular substance of the tongue supports this concept. But as our knowledge of the myoblastomas has developed it has become obvious that they sometimes occur in regions of the body where there is no muscle tissue of any sort The gum of the newborn infant is a good example We have observed several granular cell myoblastomas in this location, and there are reports of other cases

The breast is likewise without muscle tissue except for a network of smooth muscle fibers in the subareolar region and in the nipple, and encircling the terminal ducts beneath the nipple Seitz made a special study of the musculature of the breast and concluded that there is no striated muscle tissue in the breast proper A diagram showing the location of our six myoblastomas (Fig 188) makes it clear that the tumors were all far from the areolar and nipple region

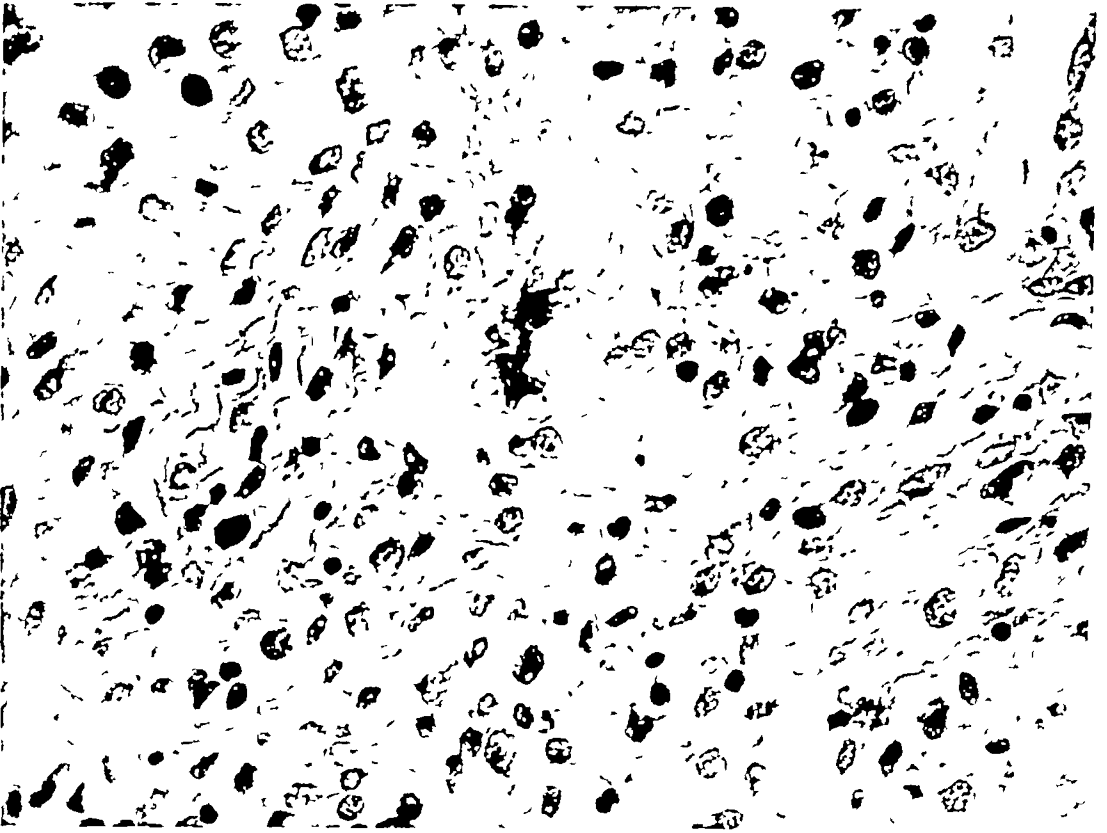


Fig 184 Microscopical appearance of liposarcoma of the breast showing myxoid stroma and bizarre giant cells

Fig. 185. Liposarcoma infiltrating a mammary lobule

concluding that these tumors do not occur in the lateral half of the breast, but the question is worth bearing in mind

The clinical importance of granular cell myoblastoma of the breast lies in the fact that it can produce all the clinical signs of early carcinoma The tumor is hard It is relatively fixed in the breast tissue surrounding it It may be abnormally attached to the underlying pectoral fascia It may cause dimpling of the overlying skin The gross appearance of the lesion is enough like carcinoma to betray most pathologists into making this diagnosis if they depend upon the gross appearance alone without taking the precaution of making a frozen section The closest scrutiny will show that myoblastoma is more sharply circumscribed than most carcinomas and that its cut surface is whiter and more uniform than the grayish

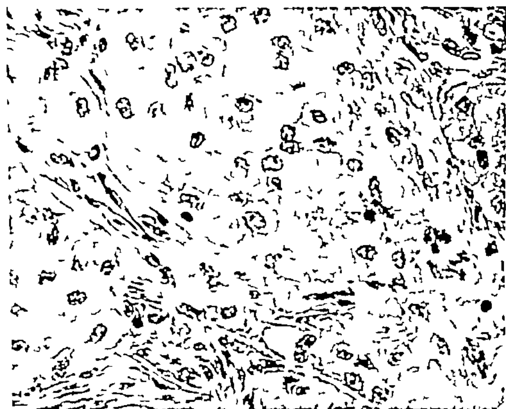


Fig 187 Microscopical appearance of granular cell myoblastoma.

chalk streaked surface of the typical carcinoma These differences, however are slight and easily missed

The similarity in gross appearance of myoblastoma and several other benign lesions that occur in the breast, to carcinoma is the reason why we biopsy every breast tumor and do a frozen section before deciding how to treat it. Myoblastoma is easily recognizable in a good frozen section In our three most recent cases, the diagnosis was made in this way

Granular cell myoblastomas have, with rare exceptions behaved as benign lesions A few undoubted malignant ones have been described, such as the one arising in the bladder reported by Ravich and Stout In our laboratory we have recently studied two more malignant myoblastomas one apparently developing in the thigh and the other on the chest wall The microscopical appearance of

Search for muscle tissue from which these tumors might have developed, therefore, turns to the musculature of the chest wall All five of our tumors appeared to have developed within the breast itself superficial to the pectoral fascia, and, therefore, superficial to the pectoralis major muscle

The occurrence of these myoblastomas adjacent to the sternum suggests a possible origin from the *sternal* muscle, a small anomalous muscle of great variability which occurs in from 1 to 10 per cent of Europeans Eisler describes this muscle as extending vertically or diagonally across the upper chest close to the sternum, superficial to the pectoral fascia



Fig 186 Gross appearance of granular cell myoblastoma

Another possible origin is from the platysma Its fibers extend in a fan-like manner down over the chest wall from the neck, as far caudally as the fourth rib These muscle fibers lie upon the superficial fascia and are, therefore, immediately adjacent to the mammary gland which lies beneath this fascia

All five of the granular cell myoblastomas of the breast that I have studied personally, and in which I know the exact site of the lesion, developed in the medial half of the breast, and may have originated from either the sternal muscle or the platysma Until more cases have been reported we are not justified in

lesions were of long duration 2 and 4 years respectively In all three patients the lesion was a small slightly elevated reddish tumor obviously developing in the skin and movable over the deeper mammary tissue It was mistaken for a sebaceous cyst in two cases

The following case illustrates this unusual lesion

F J., a housewife aged 57 came to the Presbyterian Hospital complaining of a tumor of the breast of two years duration The patient stated that the tumor varied in size and that at times it was painful and reddened and stood up like a nipple. Figure 189 shows the tumor in the radius of 11 o clock at the edge of the areola of the left breast. It was a 1 5 cm. poorly circumscribed firm lesion of the skin It was slightly elevated above the skin surface and its surface was somewhat reddened It was excised locally and proved to be a characteristic leiomyoma (Fig 190)

All three of our patients were cured by simple local excision Stout states that malignant change in this superficial type of leiomyoma is unknown

The vascular type of leiomyoma developing in deeper tissues is rarer in the breast. Striking examples of such tumors in the breast have been described however by Strong by Stein by Melnick and by Craig In these cases the tumors grew slowly over a period of years to reach a large size They were encapsulated and freely movable within the breast At the Presbyterian Hospital we have had no example of this type of mammary leiomyoma

Leiomyosarcoma

In his large series of malignant mesenchymal tumors Stout found no leiomyosarcoma developing in the breast

Rhabdomyosarcoma

This vicious tumor develops ordinarily from skeletal muscle but occasionally it is found in tissues where striated muscle is not expected Sailer and Evans have described rhabdomyosarcomas of the breast and Stout studied one in our Presbyterian Hospital data. An abstract of this one follows

M H. a housewife aged 77 came to the Presbyterian Hospital complaining of a breast tumor of two weeks duration Examination showed an 8 cm., sharply delimited round, elastic, movable tumor of the upper outer sector of the left breast. There were no enlarged axillary nodes.

After biopsy which indicated that the tumor was a sarcoma of some type and not a carcinoma, simple mastectomy with removal of the pectoral fascia was done. The tumor was grossly encapsulated and measured 6 x 5 cm. Its cut surface was firm yellowish pink, myxoid, and bulged slightly (Fig 191)

In tissue culture the tumor grew out cells which were characteristic of neoplastic striated muscle cells On the basis of this evidence and from its microscopical appearance (Fig 192) Stout classified it as a rhabdomyosarcoma.

The patient was well thirteen years later

Neurofibromatosis of the Breast

Neurofibromatosis may involve the skin and subcutaneous tissues over the breast. There seems to be a special tendency for the papillary fibromas, which are one of the features of neurofibromatosis, to develop in the areolar and nipple

these malignant myoblastomas has not differed from that of the benign lesions The only myoblastoma of the breast which has metastasized is the one described by Crawford and DeBakey It metastasized to the lungs and liver In view of our present knowledge, the proper treatment for myoblastoma of the breast would seem to be local excision

Leiomyoma

Outside of the uterus and gastrointestinal tract leiomyomas are uncommon They develop in the deeper tissues from the smooth muscle of blood vessels and

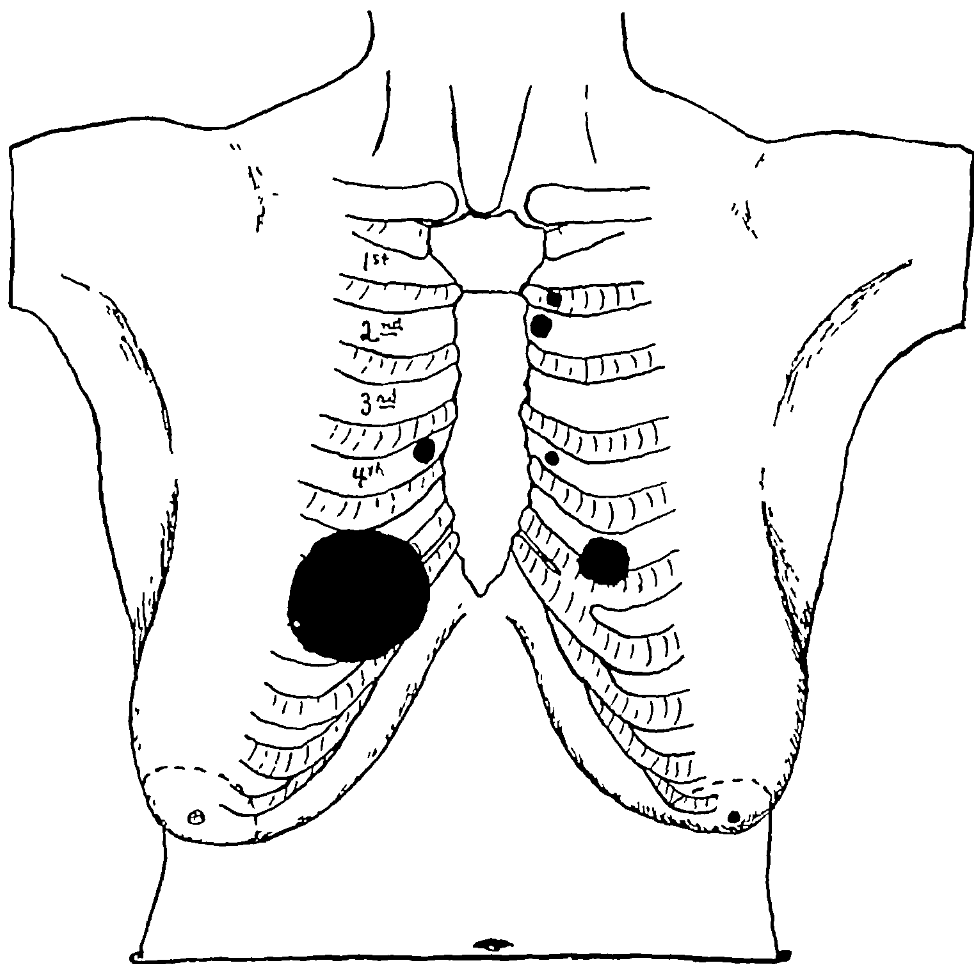


Fig 188 The location of the six granular cell myoblastomas in our personal series

can be classed as *vascular leiomyomas*, or from the smooth muscle of the skin, as *superficial leiomyomas*

In the breast *superficial* leiomyomas have occasionally been observed arising in the skin of the areolar region Melnick collected reports of 10 such tumors There is, of course, a well developed layer of smooth muscle in the corium of the areolar region, from which leiomyoma might arise Contraction of this smooth muscle is readily observed upon stimulation of the nipple or areola

At the Presbyterian Hospital we have had three examples of this superficial type of leiomyoma Two were in the skin of the areola and the third in the skin of the upper inner sector of the breast, several centimeters from the areola

Our patients were 25, 50, and 57 years of age, respectively In two of them the

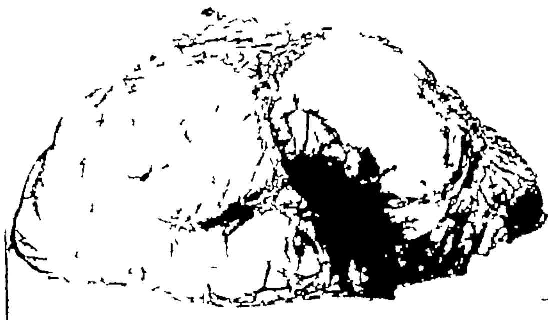


Fig 191 The gross appearance of rhabdomyosarcoma of the breast.

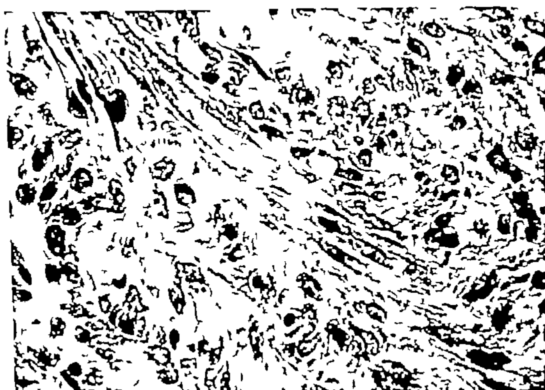


Fig 192 The microscopical appearance of rhabdomyosarcoma of the breast.

area Striking cases of this kind have been described by Schilling and by Ottow We have had a good example in the Presbyterian Hospital

Miss D H came to the Presbyterian Hospital at the age of 29 complaining of a tumor of her tongue She had the fully developed syndrome of neurofibromatosis, with typical café-au-lait spots on her skin (Fig 193) numerous small pedunculated cutaneous neurofibromas, and several subcutaneous neurofibromas. She had in addition two



Fig. 189. Superficial leiomyoma of the areolar region.

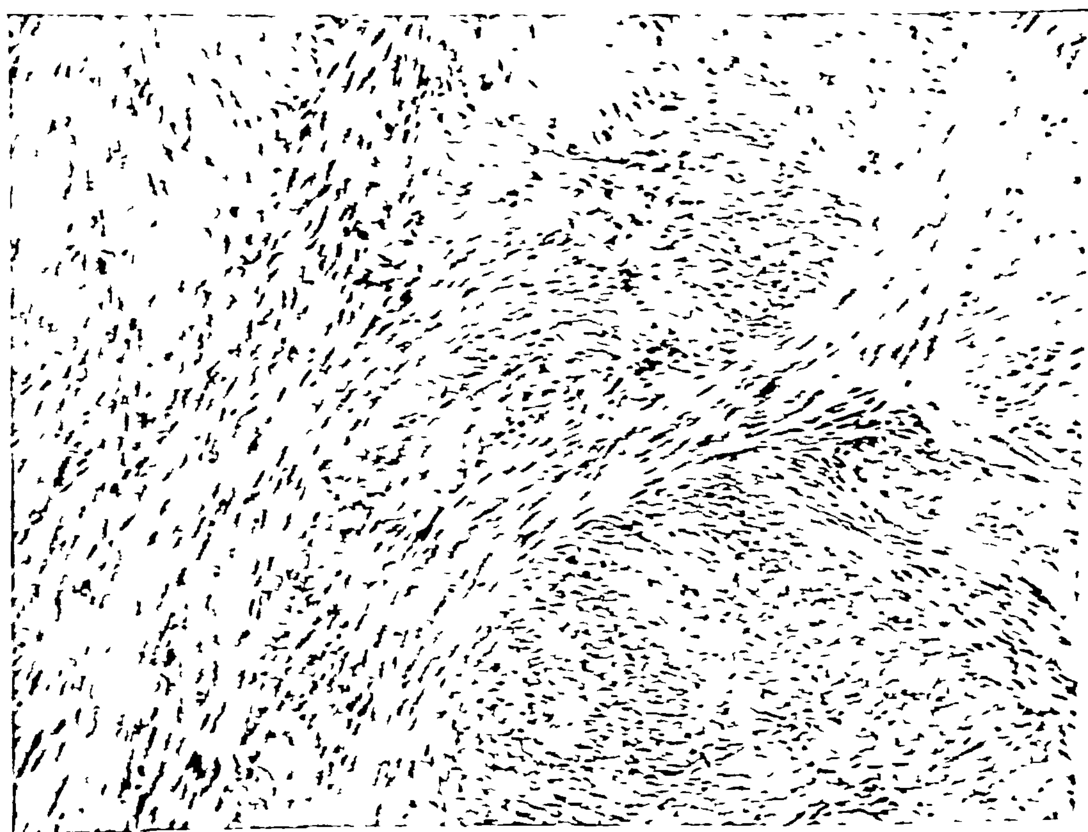


Fig 190 Microscopical appearance of superficial leiomyoma of the areolar region

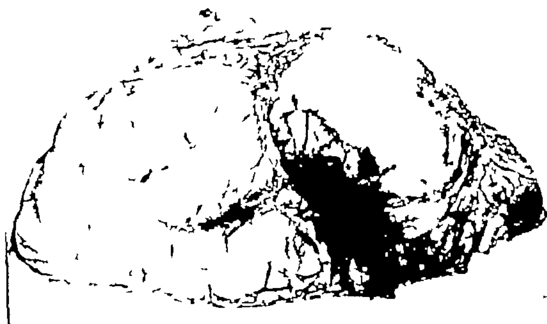


Fig. 191 The gross appearance of rhabdomyosarcoma of the breast.

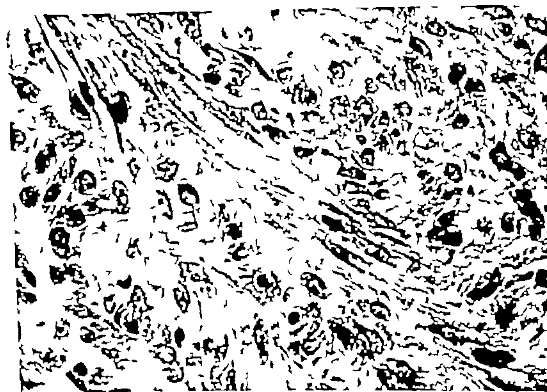


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typical neurofibromatous lesions (1) Along the left side of her tongue there was a thick, submucous mass of neurofibromatous tissue (2) There was a cluster of elevated and pedunculated neurofibromas projecting from the areolas and nipples bilaterally

During the ten years following her admission the patient's nipple lesions slowly increased in size Individually some of the papillomas became as large as 2 cm in length Figure 194 shows their appearance They were so disfiguring and troublesome that excision of the papillomas and plastic reconstruction of the nipples was performed Pathologically the lesions were characteristic neurofibromas

Malignant Hemangioendothelioma

Stout prefers the name hemangioendothelioma, originally given by F B Mallory, for the highly malignant rare type of sarcoma that develops from the

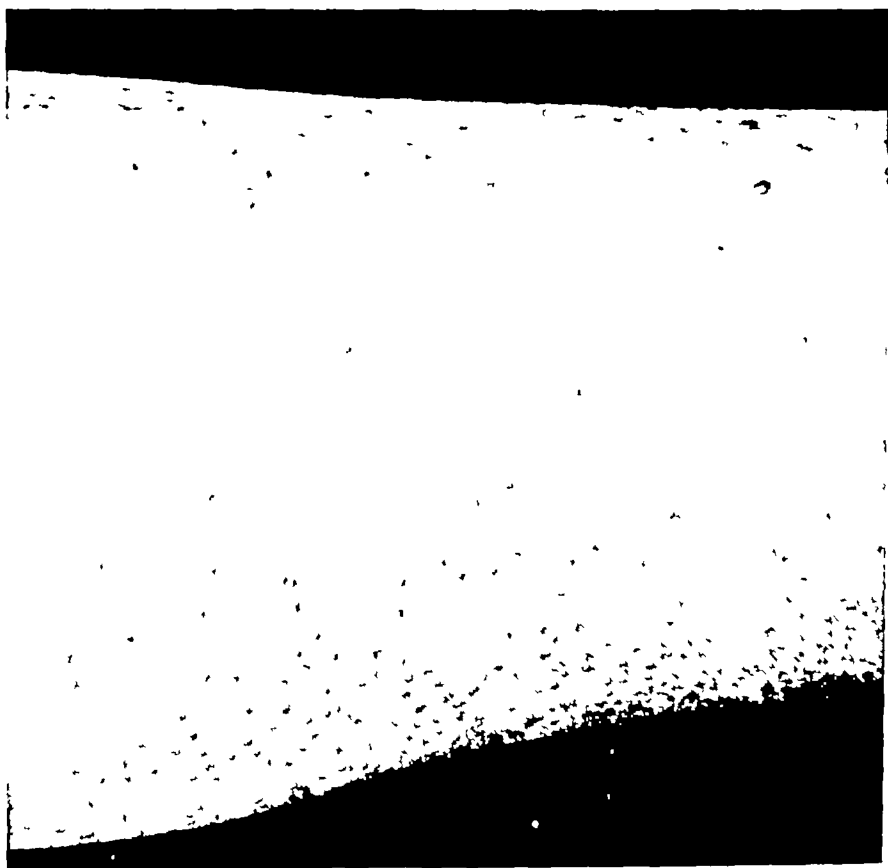


Fig 193 Characteristic cafe-au-lait spot on the arm of a patient with neurofibromatosis of the breasts

endothelial lining cells of blood vessels He has studied 4 such tumors developing in the breast A series of 6 such cases has recently been reported by McClanahan and Hogg Individual cases have been described by Robinson and Castleman, Enticknap, T B Mallory, and Tibbs

With the exception of two patients aged 65 and 68, respectively, whose tumors were described by Stout, all of the women with this type of tumor in the breast have been young, three being in their late teens and seven in their twenties The lesion grows rapidly to form a bulky breast tumor Its vascular character is suggested by the bluish-red appearance of the overlying skin It does not involve the regional lymph nodes, but metastasizes widely to the viscera, and is rapidly fatal. Both surgery and irradiation are entirely futile

The following is an abstract of the history of one of our Presbyterian Hospital cases It is typical of the history of malignant hemangioendothelioma

J M an 18 year old girl came to the Presbyterian Hospital complaining that two months previously she had noted a "blue mark in the areola of the right breast. For one week there had been a tumor beneath the blue mark

The right breast was slightly enlarged and the nipple inverted There was bluish dis coloration of the upper half of the areola Beneath this discoloration there was a firm, rounded freely movable tumor 6 x 3 cm in diameter

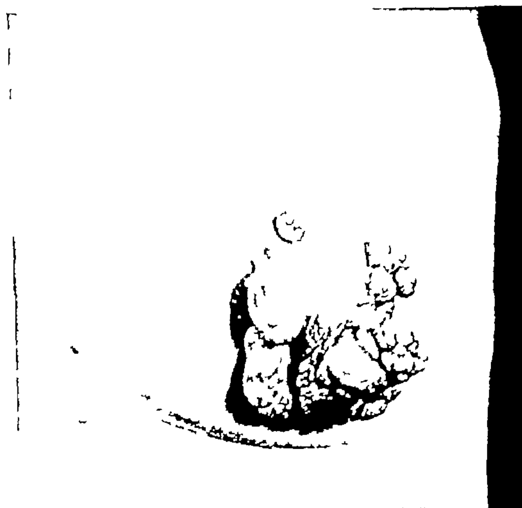


Fig 194 Pedunculated neurofibroma of the nipple region

Under the direction of a gynecological consultant the patient was treated with estrogen under the illusion that the breast lesion represented a functional condition.

The tumor continued to enlarge. An infrared photograph taken nine months after her first admission (Fig 195) showed its vascular character It appeared as a dark area visible through the skin of the areolar region. Its vascular character was further con firmed by the fact that upon pressure with the patient supine the volume of the tumor markedly diminished.

During the succeeding six months the tumor grew rapidly to the massive size shown in another infrared photograph (Fig 196) A simple mastectomy was then done. Pathological study showed the lesion to be a malignant hemangioendothelioma. Figure 197 is a high power view of its microscopical appearance, and shows anaplastic endothelioblasts filling atypical capillaries.

A metastatic tumor nodule in the abdominal wall, and widespread bone metastases developed shortly after operation, and the patient died twenty months after the onset of her disease There was never any clinical evidence of involvement of regional lymph nodes

Lymphangiosarcoma

The extreme degree of lymphatic stasis that results from marked edema of the arm when poor wound healing follows radical mastectomy gives rise to a special form of sarcoma, apparently arising from the endothelial lining cells of the lymphatics



Fig 195 Malignant hemangioendothelioma of the areolar region as seen in an infrared photograph

Stewart and Treves were the first to identify this lesion, which has a superficial resemblance to Kaposi's sarcoma Purplish-red macules and papules appear in the skin of the edematous arm They enlarge, coalesce, and eventually become cystic and necrotic Pulmonary metastases finally occur Stewart and Treves included 6 cases in their original report Others have been described by Jessner et al, by Vos, by Hall-Smith and Haber, by Ferraro, by Rawson and Frank, by Froio and Kirkland, and by Cruse et al Stout has studied 7 of these tumors One of these patients, whom we observed, had the following history

M C, aged 55, an Irish housewife, had a left radical mastectomy in another hospital, in September, 1937 She was given prophylactic postoperative irradiation from October, 1937 to April, 1938

In May, 1938, local recurrence was noted and additional irradiation was given to the recurrence In August, 1938, local excision of part of the irradiated area was done in another hospital with slow wound healing

The arm had become markedly edematous by this time, and the edema persisted and increased.

She consulted me in April 1950 because of purple spots which had developed in the skin of the upper part of the edematous arm They had first appeared a year previously and had recently progressed

Her condition when I examined her is shown in Figure 198 There was an old mastectomy scar of the type that is carried out onto the anterior aspect of the upper arm There were marked irradiation changes in the skin along the whole length of the scar but these changes were most marked over the upper portion of the scar on the anterior aspect of the shoulder

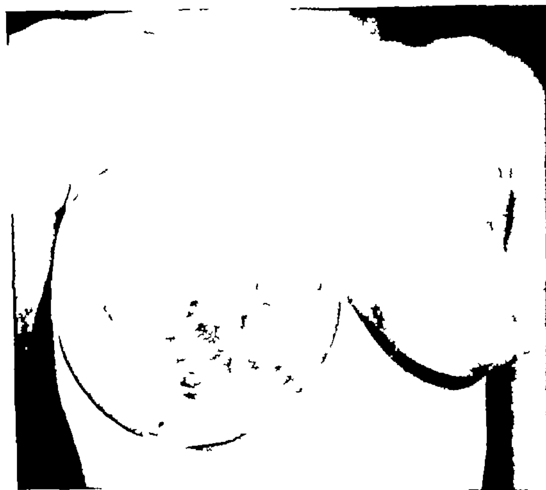


Fig 196 Malignant hemangioendothelioma at a later stage as seen in an infrared photograph.

The whole arm was markedly edematous, the tissues being firm and the skin thickened On the anterior aspect of the upper arm beginning just distal to the outer limits of *irradiation changes in the skin* there were isolated and confluent groups of purplish, slightly elevated macules. In the center of the largest group of macules there was an elevated, soft, purplish tumor nodule measuring 2 cm in diameter Biopsy of the nodule showed the characteristic microscopical picture of lymphangiosarcoma (Fig 199) In some portions of the tumor malignant endothelioblasts were seen growing in the walls of dilated lymphatics (Fig 200)

Interscapulo-thoracic amputation was advised but the patient refused and went elsewhere

The origin of these lymphangiosarcomas must be related to the marked degree of lymphedema that has been present in all the cases The duration of the edema

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by Thür and by Pohl Kay has reported a remarkable case in which the disease developed in a woman aged 28 following pregnancy Both breasts were symmetrically involved and grew very large before death with cerebral disease We have only one example of primary lymphosarcoma of the breast in the Presbyterian Hospital data A summary of this patient s history follows

Mrs. I B a 65 year old Scottish widow came to the Presbyterian Hospital because of a tumor in her right breast She had discovered it one year previously At that time



Fig 198 Lymphangiosarcoma developing in an edematous arm thirteen years after radical mastectomy

it was a small, firm tumor situated just lateral to the areola It steadily enlarged. Six months previously the skin over it had ulcerated Three months previously she had first noticed a tumor in her right axilla.

Examination showed a large ulcerated tumor in the right breast situated in the upper half of the breast (Fig 201) The edges of the ulcer were raised and crenelated Its base was necrotic. The lesion was situated superficially in the breast and did not extend down in the breast substance more than 2 or 3 cm. Its edges were remarkably well defined in the breast tissue. The breast as a whole was freely movable over the chest wall.

In the axilla there was a massive group of enlarged nodes, 8 cm. in diameter fixed in the deeper structures of the axilla. Palpation of the infraclavicular region gave a

before the lymphangiosarcoma developed has varied from six to twenty-four years in the 13 cases thus far reported (including our own) Only 9 of the patients had had irradiation so that the irradiation in itself cannot be held responsible

The treatment in most of the cases has been interscapulo-thoracic amputation This has been unsuccessful Rawson and Frank treated their patient by irradiation and report that the lesion was radiosensitive and that the patient is well after one year

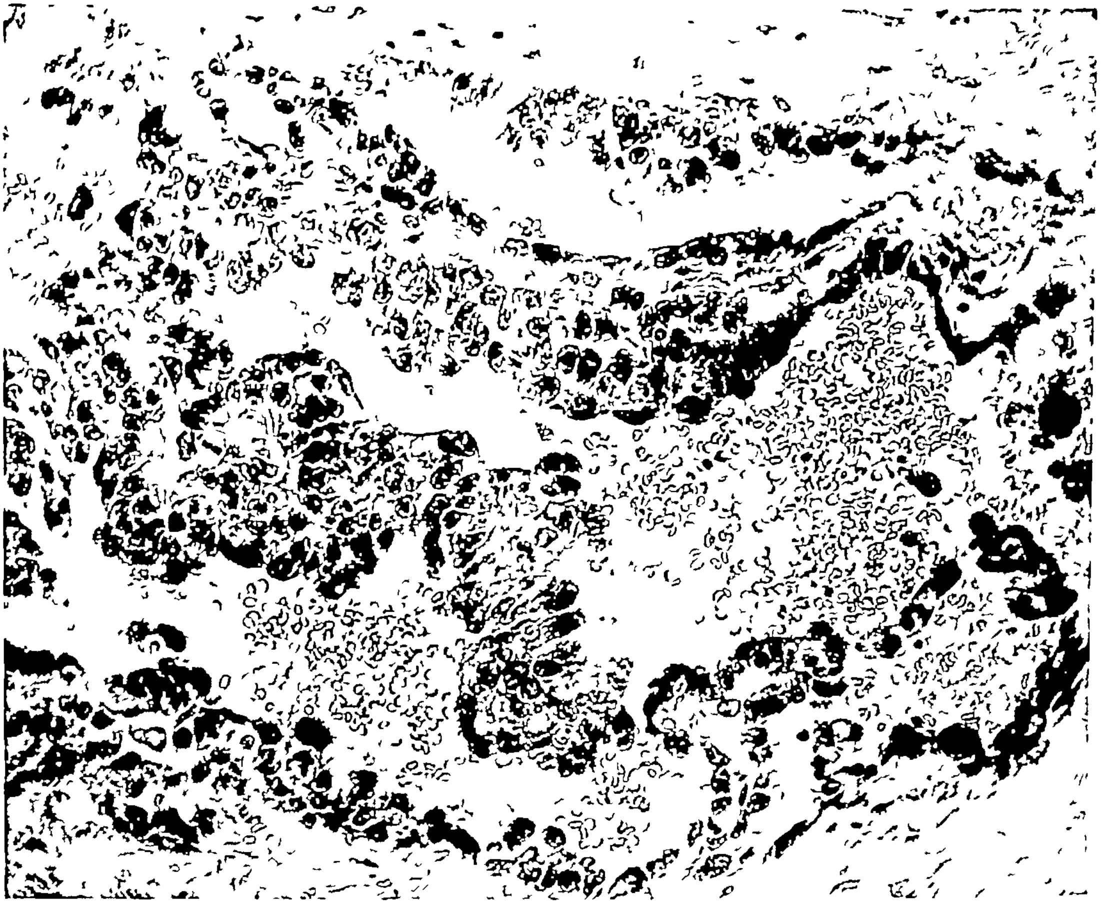


Fig 197 Microscopical appearance of malignant hemangioendothelioma showing anaplastic endothelioblasts filling atypical capillaries

Lymphoblastoma

All types of lymphoblastoma have appeared in the breast as primary manifestations, without concurrent manifestations of the disease elsewhere In such cases the disease soon appears in other areas of the body, in lymph nodes, etc and follows its characteristic course The primary mammary manifestation in the breast is often mistaken for carcinoma, if biopsy is not done, and a futile radical mastectomy performed This type of disease is therefore another example of the necessity of biopsy before radical mastectomy

Benign lymphocytoma of the breast, which did not evolve into lymphosarcoma, has been reported by Kreitner and Ulm In our Presbyterian Hospital data we have no example of this condition

Lymphosarcoma, appearing primarily in the breast, has been well described

sensation of fullness in the upper axilla. There were no palpable supraclavicular nodes. No enlarged lymph nodes could be palpated anywhere else in the patient. The chest film was negative. Skeletal films showed no definite evidence of metastasis.

Biopsy of the ulcerated tumor of the breast showed reticulum cell lymphosarcoma (Fig 202)

The lesion was treated with radiation and disappeared entirely within a month after treatment had begun.

Hodgkin's Disease

Hodgkin s disease manifests itself in the breasts with great rarity We have no example of this breast lesion in Presbyterian Hospital data Kückens was the



Fig 201 Lymphosarcoma of the breast

first to report such a lesion It occurred in a sixteen year old girl A tumor re moved from the upper portion of her breast proved to be typical Hodgkin s disease In 1945 Adair and his associates described five cases, among a total of 406 with Hodgkin s disease in which tumors of the breast were presumed to be Hodgkin s disease Microscopical proof that the breast lesion was indeed Hodg kin s disease was available in only two of these cases More recently well docu mented additional cases have been described by Koeppler and by Bertrand and Lataix A very interesting case has been described by Randall and Spalding The patient aged 28 had had a breast tumor for ten years which grew during preg nancy and lactation The clinical picture was that of carcinoma and radical

Fig 199 Microscopical appearance of lymphangiosarcoma of the arm

Fig 200 Malignant endothelioblasts growing in the wall of a dilated lymphatic in lymphangiosarcoma of the arm

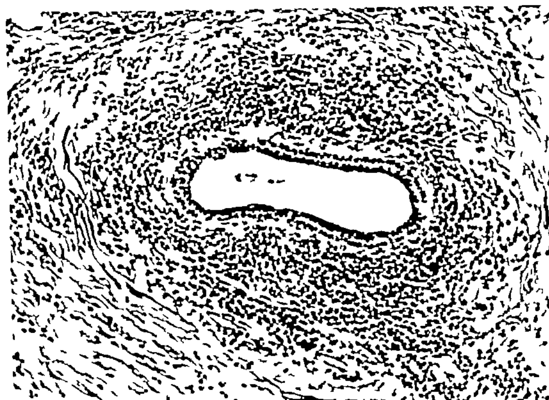


Fig 203 Leukemic infiltration around a mammary duct.

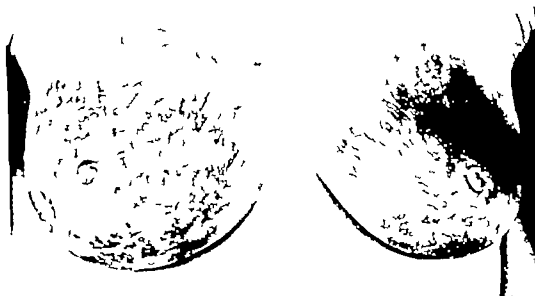


Fig 204 Myelogenous leukemia involving both breasts.

mastectomy was done Both the primary lesion in the breast and its axillary metastasis proved to be typical Hodgkin's disease

Leukemia

Leukemia manifests itself as an infiltration of the breast in occasional cases McWilliams and Hanes reported such a case from our hospital in which bilateral radical mastectomy was done Gelin et al described one in which the breast lesion simulated an abscess

In a patient of mine, whose history follows, I could not differentiate clinically between the inflammatory type of carcinoma and leukemia

L C, an unmarried nurse aged 49, began to have chills, anorexia, nausea, and some vomiting, night sweats and general malaise, in April, 1942 She had intermittent fever

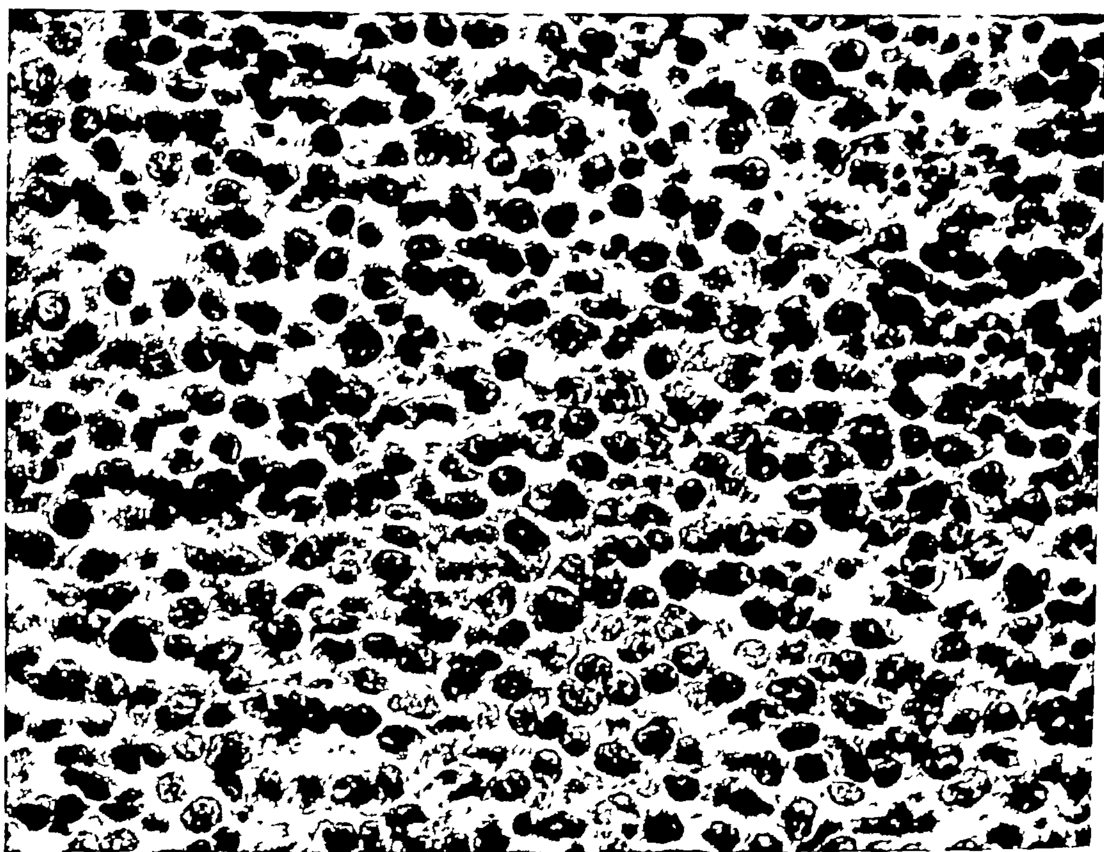


Fig 202 Microscopical appearance of reticulum cell lymphosarcoma of the breast

of between 100° and 103° Erythematous nodules appeared on her lower legs Blood studies were at first not remarkable, but by the middle of May a few immature white cells resembling blasts began to be seen

At this time a lesion developed in her right breast The breast was considerably enlarged by a diffuse induration involving its lower portion The skin was red, abnormally warm, and showed early edema The lesion was tender There were no enlarged regional lymph nodes The clinical picture resembled that of the inflammatory type of carcinoma, or a low grade inflammatory process of some sort The blood picture, however, suggested leukemia While the diagnosis was being debated the lesion on the right side extended to involve most of the right breast, and a similar lesion appeared in the upper central part of the left breast A biopsy was then done upon the right breast, and myelogenous leukemia found (Fig 203) The appearance of the breasts at this time

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is shown in Figure 204 Irradiation was given to the breast lesions without much response The patient failed rapidly, leukemic infiltration developed in many body areas, and she died 6/29/42

There are several clinical features that are apparently common to lymphoblastoma developing in the breast The lesions are, first of all, often bilateral. They are often superficially situated in the breast and many involve the skin The retraction signs, regularly seen with carcinoma, are not present

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CHAPTER 15

TUMORS OF THE SKIN AND THE ACCESSORY GLANDS OF THE SKIN OVER THE BREAST

Any of the lesions that develop in the skin and from its accessory glands may of course appear in the skin over the breast Their only special interest in this situation is their simulation of lesions of the mammary gland For this reason it seems worth while to present examples of several of these lesions of the skin of the breast that I have seen

Epithelioma

Epitheliomas are unusual in skin over the breast, perhaps because this area gets so little ultraviolet light We have only two examples in our Presbyterian Hospital data Both were basal cell epitheliomas One of these is summarized as follows

Mrs H W developed a lesion of the skin of the right mammary region when she was 62, fifteen years after bilateral radical mastectomy, performed for bilateral primary mammary carcinoma

There was no evidence of recurrent or metastatic mammary carcinoma The skin of her thorax, both in front and in back, showed scattered senile keratoses

In the skin of the right mammary region, just lateral to the vertical mastectomy scar, there was a scaly, reddish, slightly raised, 2 cm lesion Biopsy showed it to be a basal cell epithelioma It was treated with irradiation and had not recurred eleven years later when she was last seen

Sweat Gland Adenoma

Since sweat glands are found in the areola and skin over the breast, neoplasms might be expected to develop from them They are rare, however, and apparently always benign Moulonguet and Erjavec have described a sweat gland adenoma of the areola, and I dealt with one of these tumors developing in skin over the breast A summary of the features of my case follows

M H , an adolescent Negress aged 16, came to the Presbyterian Hospital complaining of a tumor of the left breast Eighteen months previously she had first noted a "pimple" in the skin over the lower inner sector of the breast It had steadily increased in size and finally become ulcerated

The appearance of this lesion is shown in Figure 205 It was a firm papillary tumor 2 5 cm in diameter, projecting 1 cm above the surrounding skin Its surface was ulcerated

It was excised with an ellipse of surrounding skin and proved to be a sweat gland adenoma (Fig 206) There had been no recurrence thirteen years later

Sebaceous Cyst

Sebaceous cysts are not uncommon in the skin over the breast. Here, as elsewhere, they are recognized by their superficial situation their circumscribed character and by the dilated sebaceous duct orifice in the overlying skin

There are two special points to be noted regarding the diagnosis of sebaceous cyst of the skin over the breast At the periphery of the mammary gland, particularly along its medial border where it extends as a very thin sheet almost to the midline of the sternum, a small carcinoma lies so close to the skin surface that it



Fig. 205 Sweat gland adenoma projecting from the lower portion of the breast.

simulates a sebaceous cyst and has often been mistakenly locally excised without the surgeon having any suspicion that he was dealing with carcinoma.

Sebaceous cysts in the skin over the breast, when they become infected may be accompanied by a considerable amount of induration and by such well developed signs of inflammation that abscess or even the inflammatory type of carcinoma is suggested Figure 207 shows such an infected sebaceous cyst of the skin over the breast, occurring in a woman aged 44 who came to the Presbyterian Hospital complaining of a tender tumor of the breast of one week s duration. The tumor measured 2 cm in diameter and was firm but not hard The skin over

Fig 206 Microscopical appearance of sweat gland adenoma of the skin over the breast



Fig 207 Infected sebaceous cyst of breast

it was red It was locally excised and the wound closed with a small drain left in place for forty-eight hours

Moles and Nevi

Moles, either pigmented or non pigmented may develop in the skin over the breast There is of course no more reason for excising them from the skin over the breast than elsewhere However when moles enlarge and become darker in color the suspicion of melanoma arises The most deceptive lesion in this class is the so-called epidermoid type of nevus It may simulate a melanoma and lead the surgeon to unnecessarily radical surgery as in the following case

A. B., a housewife aged 64 came to the Presbyterian Hospital complaining of a tumor of the skin of her right breast. She had had a black spot in the skin over the breast for many years. Four weeks previously it had begun to enlarge and had ulcerated.

Examination showed a slightly raised tumor of the skin just medial to the areola of the right breast (Fig 208) The medial half of the surface of the lesion was covered by

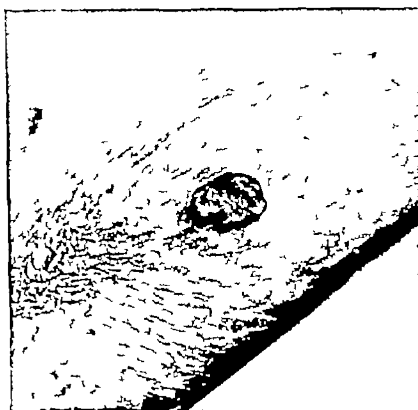


Fig 208 Papillary epidermoid nevus of skin of breast

intact epithelium and was bluish-black. The lateral half of its surface was ulcerated. There were no enlarged axillary nodes. I assumed that the lesion was a melanoma, and not wishing to biopsy it for fear of producing metastases, I performed a simple mastectomy and an axillary dissection. To my surprise the lesion was only a papillary epidermoid nevus or so-called seborrheic keratosis

Melanoma

In our Presbyterian Hospital data the only example of a malignant melanoma developing in the skin over the breast was one which I treated A summary of this case follows

Fig 206 Microscopical appearance of sweat gland adenoma of the skin over the breast



Fig 207 Infected sebaceous cyst of breast

E. H., a housewife aged 63 came to the Presbyterian Hospital for a tumor of her right nipple. She had had a "reddish-brown wart" the size of a pea, close to her right nipple for eighteen years without any change in its size or color One month previously it had begun to enlarge, and changed from its original reddish brown to black One week previously its surface had "cracked" and since then it had bled intermittently

From the surface of the right nipple and the adjacent areola a black elevated lesion projected (Fig 209) It measured 2 3 cm. in diameter Its surface was irregular and crusted. There was a moderately enlarged movable lymph node in the right axilla. A chest film was negative and no melanin was found in the urine.

A diagnosis of malignant melanoma was made, and a radical mastectomy was performed. No preliminary biopsy was done because of the fear of producing metastases. Study of the operative specimen confirmed the diagnosis of malignant melanoma (Fig. 210) There were metastases in 2 of 15 axillary lymph nodes.

Three years later the patient developed anorexia, weakness, and left epigastric fullness. There was free fluid in the abdominal cavity and a mass in the left lower quadrant. At exploratory laparotomy the peritoneal cavity was found to be studded with black nodules of metastatic melanoma The patient died 46 months after her first symptom of melanoma.

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Moulonguet, P and Erjavec. Les tumeurs bénignes des glands mammaires accessoires rétro-aréolaires. J Chir 67:689 1951



Fig 209 Malignant melanoma of the nipple region

Fig 210 Microscopical appearance of malignant melanoma of nipple region

it was before antibiotics were available, because physicians are now tempted to try to abort presumed breast abscesses with antibiotics without incising them

It is certainly not safe to attempt to distinguish a low grade breast abscess from a carcinoma with accompanying signs of inflammation on the basis of clinical evidence alone I suggest two rules to prevent this error

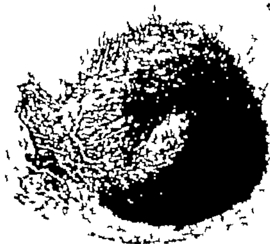


Fig 211 Typical lactation abscess.

1 Abscess is very uncommon except in women who have recently lactated. In all other patients a tumor accompanied by redness of the skin and other signs of inflammation should be presumed to be due to duct ectasia, to subareolar chronically recurring infection, or to carcinoma

2. Since good surgical practice has shown that any accumulation of pus should be evacuated even though antibiotics are used a presumed breast abscess should always be incised and drained. The incision need only be a small curved one made in the skin lines, and not a radial incision When this is done a biopsy should always be taken of any indurated area In this way a carcinoma will not be missed

Subareolar Chronically Recurring Abscess There is a special type of low grade infection in the breast that develops in the subareolar or juxta

CHAPTER 16

INFECTIONS IN THE BREAST

Most of the infections that occur in human tissues may localize in the breast, where the chronic types of infection may be distinguished only by the fact that since the blood supply of the breast is comparatively poor, their course may be unusually indolent I do not propose to deal with their diagnosis in detail, but only to point out some of the main features of the more frequent types of infection

Abscess

Lactation Abscess. Women who are nursing not infrequently develop areas of tenderness in the breast, accompanied by some degree of induration, slight redness of the skin, and a minimal systemic reaction Stopping nursing from the affected breast, with bed rest, and the administration of a broad spectrum antibiotic for a few days often controls such limited infections, and nursing may be resumed When the inflammatory reaction does not subside but persists and increases, and localizes to form a tumor, it usually represents an abscess Figure 211 shows the characteristic features of a lactation abscess which developed in a 19 year old mother, three weeks after lactation had been suppressed with the application of a binder and by dehydration In a patient like this, with acute pain, tenderness, and marked redness and edema of the overlying skin, the diagnosis is obvious

But redness, and elevation of the temperature of the skin over the tumor, and edema of the skin, may also accompany carcinoma, and the distinction between infection and malignancy must be kept in mind I will deal with the so-called inflammatory type of carcinoma, in which these local signs are prominent, in Chapter 24 Redness of the skin of limited extent, occurring without the other characteristic features of the inflammatory type of carcinoma, is, however, occasionally a feature of the more prosaic types of carcinoma It was observed in 74, or 7 9 per cent, of 947 carcinomas of the breast treated by radical mastectomy in the Presbyterian Hospital between 1915 and 1942 Such redness of the skin is sometimes due to necrosis or infection within the carcinoma, or to carcinomatous involvement of the overlying skin and impending ulceration, but in other cases its cause remains obscure The important point concerning redness of the skin is that it suggests infection and has often betrayed physicians into mistaking carcinoma for an abscess The mistake is more frequent today than

it was before antibiotics were available, because physicians are now tempted to try to abort presumed breast abscesses with antibiotics without incising them

It is certainly not safe to attempt to distinguish a low grade breast abscess from a carcinoma with accompanying signs of inflammation on the basis of clinical evidence alone I suggest two rules to prevent this error



Fig 211 Typical lactation abscess.

1 Abscess is very uncommon except in women who have recently lactated In all other patients a tumor accompanied by redness of the skin and other signs of inflammation should be presumed to be due to duct ectasia to subareolar chronically recurring infection, or to carcinoma.

2 Since good surgical practice has shown that any accumulation of pus should be evacuated even though antibiotics are used a presumed breast abscess should always be incised and drained The incision need only be a small curved one made in the skin lines and not a radial incision When this is done a biopsy should always be taken of any indurated area. In this way a carcinoma will not be missed

Subareolar Chronically Recurring Abscess There is a special type of low grade infection in the breast that develops in the subareolar or juxta

areolar area and forms a comparatively small localized abscess, which usually ruptures spontaneously and subsides, only to repeat the same cycle over and over again at intervals of a few months This type of abscess usually has no relationship to lactation, although it develops in younger or middle-aged women In some cases a sinus persists and the lesion flares up only when the sinus closes off The usual methods of incision and drainage, and the administration of an antibiotic appropriately chosen on the basis of sensitivity tests, regularly fail to cure this lesion The reason simple drainage fails is that these subareolar abscesses communicate with one or more of the collecting ducts at the base of the nipple. Re-infection from the outside through the nipple ducts occurs in the dense fibrous tissue at the site of the original abscess The only treatment that succeeds is a procedure developed by my associate, David Habif In a quiescent phase of the lesion, he excises the area of fibrous tissue, together with the communicating collecting duct in its entirety, out to the surface of the nipple

Tuberculosis of the Breast

Tuberculosis of the breast is perhaps less frequent than it was a generation ago when tuberculosis was more ubiquitous The diagnosis may be made less often because modern pathologists have come to realize that a great variety of granulomatous processes, including sarcoid and fungus disease, produce microscopical pictures indistinguishable from tuberculosis In our laboratory, at least, the diagnosis is not now made without clinical findings which make the diagnosis presumptive, such as proven tuberculosis of the cervical or axillary nodes or subjacent chest wall, or when tubercle bacilli are demonstrated in the breast lesion, or guinea pig inoculation is positive With these restrictions the diagnosis was made only four times in our laboratory between 1938 and 1955, during which approximately 6,500 lesions of the breast were studied This frequency can be contrasted with reports of a generation ago, such as those of Cheever, and Shipley and Spencer, who found that about 1 5 per cent of the breast lesions seen in their clinics were tuberculosis

The best recent discussion of tuberculosis of the breast is that of McKeown and Wilkinson They describe 5 undoubted cases, dividing them into "primary" and "secondary" types The primary cases are those in which the breast lesion is the only apparent manifestation of tuberculosis, the patients being in good general health McKeown and Wilkinson's 2 patients with the primary type of lesion were young women in whom the breast tuberculosis occurred in association with pregnancy The secondary cases are those in which there is chronic tuberculosis elsewhere in the body In these patients the focus in the breast often develops consequent to tuberculous involvement of axillary lymph nodes or as the result of penetration of chest wall tuberculosis into the breast

The clinical features of tuberculosis of the breast which help to differentiate it from carcinoma are that it usually occurs at an earlier age, and in patients who have other foci of tuberculosis Pain is a more prominent symptom in tuberculosis The lesion progresses more rapidly than most carcinomas, and breaks down and forms fistulae Discharge from the nipple is also more frequent than in carcinoma Leborgne has described what he regards as the radiographic features of tuberculosis of the breast Despite these differentiating features

tuberculosis is not infrequently mistaken for a carcinoma and radical mastectomy done. This is another argument for never omitting biopsy before performing radical mastectomy.

The following case illustrates the clinical features of tuberculosis of the breast.

Mrs. L. F. a colored housewife aged 21 came to the Presbyterian Hospital with a tumor of the right breast. Her disease had begun with a sharp inspiratory pain under the breast two months previously. This called her attention to the tumor. It had doubled in size since she had discovered it. She had lost 10 pounds in the previous three months.

Examination showed a thickening over the fifth right costochondral junction. From this thickening a sessile tumor extended upwards into the lower middle sector of the breast. It measured 5 cm. in diameter and was round and seemingly encapsulated. I thought it fluctuant. There were no palpable axillary nodes. X ray films showed a bulbous expansion of the anterior end of the fifth rib with a central area of radiolucency. There was no evidence of pulmonary tuberculosis.

At operation the tumor was exposed and a small incision made into it which showed that it contained caseous and purulent material. The process was firmly attached to and seemed to originate from the chest wall in the region of the fourth interspace and the 5th costochondral junction. This area of the chest wall and the costal cartilage and rib were excised in continuity with the tumor. Microscopically it proved to be a tuberculous abscess originating from tuberculosis of the rib.

The patient recovered without incident. Five years later she went through a pregnancy normally. It is interesting to note, however, that eleven years after her chest wall tuberculosis had been excised she developed pulmonary tuberculosis.

Coincident Carcinoma and Tuberculosis of the Breast

Carcinomas and tuberculosis of the breast are occasionally found coincidentally in the same patient. In 1926 Smith and Mason collected reports of 18 such cases and described one that they observed. Schultze Jena recently has reported four such cases. More recently Grausmann and Goldman have described two other indubitable cases. The rare finding of carcinoma in one breast and tuberculosis in the other has been described by Scherer. Villard and Martin reported one case in which the two diseases coexisted not only in the breast but in the axillary lymph nodes. The latter finding is not rare. In our laboratory we have found microscopical tuberculosis in axillary lymph nodes as well as axillary metastases of carcinoma in a number of cases. The old concept that the two diseases are antipathetic to each other is certainly unsound.

Sarcoid of the Breast

The localization of sarcoid in the breast is very unusual even in the northern European countries where sarcoid is more frequent. Scott, as well as Stallard and Tait, have reported single cases from England, and Dalmark has described a third case from Denmark.

At the Francis Delafield Hospital we have had two patients with sarcoid involving the breast. The case histories of these patients follow.

Case 1 Mrs. A. v. de E. a middle-aged woman of German origin, was admitted to the hospital in April, 1952, because of a lesion of the skin of the left breast. It had been

first noted two years prior to admission It began as an eczema-like manifestation involving a small area of the skin above the nipple It itched and she scratched it a good deal It responded temporarily to topical applications but after a period of quiescence the lesion extended until it involved the skin over the entire breast

Examination on admission revealed no abnormalities other than the lesion of the breast The *skin over the entire left breast was thickened, indurated, roughened, and reddened* There were scattered areas of shallow ulceration covered with foul smelling exudate and crusts The areola and nipple were intact Figure 212 shows the appearance of the lesion No mass could be palpated in the breast A single enlarged but movable lymph node was felt in the mid-axilla on the side of the lesion



Fig 212 Sarcoid involving the skin over the entire breast Appearance on admission

Several biopsies of different portions of the lesion were taken Microscopical study revealed a striking granulomatous inflammation characterized by tubercles containing giant cells, but without caseation or necrosis No acid-fast bacilli could be demonstrated The final diagnosis was sarcoid

The laboratory data were within normal limits A chest rœntgenogram was negative Cultures from the lesion revealed various organisms including Pseudomonas aeruginosa, non-hemolytic streptococcus, B pyocyaneus, Staphylococcus aureus and diphtheroids At no time were acid-fast bacilli demonstrated

The lesions proved to be refractory to parenteral antibiotic therapy but were somewhat improved by topical applications of neomycin. The ulcerations finally healed. The

residual lesion consisted of a patchy induration and discoloration of the skin. On follow up examination it became obvious that the lesions were showing spontaneous improvement as time went by No specific therapy has been prescribed. Figure 213 shows the appearance of the breast three years after admission

Case 2 S C. a 53 year old colored woman was admitted to the hospital because of a lump in the left breast of two years duration Inquiry revealed no symptoms other than a progressive exertional dyspnea and a paroxysmal cough

On physical examination her blood pressure was 200/120 A hard mass was palpable in the upper outer quadrant of the left breast with retraction of the overlying skin. An



Fig 213 Sarcoid of the skin of the breast. Appearance after three years.

enlarged node was felt in the left axilla and palpation of the neck and groins revealed a diffuse lymphadenopathy The heart was enlarged but no abnormal physical findings were demonstrated in the lungs

Serologic tests were positive for syphilis A chest roentgenogram revealed cardiac enlargement, widening and calcification of the aorta, and an extensive infiltrative process in the right lung, with atelectasis of the right upper lobe

The tuberculin skin test was negative and several sputa were negative for acid fast bacilli and tumor cells Biopsy of the breast tumor and the internal mammary nodes in the upper three interspaces was performed The breast tumor was a carcinoma. The internal mammary nodes contained no carcinoma, but a node from the first interspace showed sarcoid. A left radical mastectomy was done. The microscopical examination of the operative specimen revealed sarcoid in both the mammary gland and the axillary

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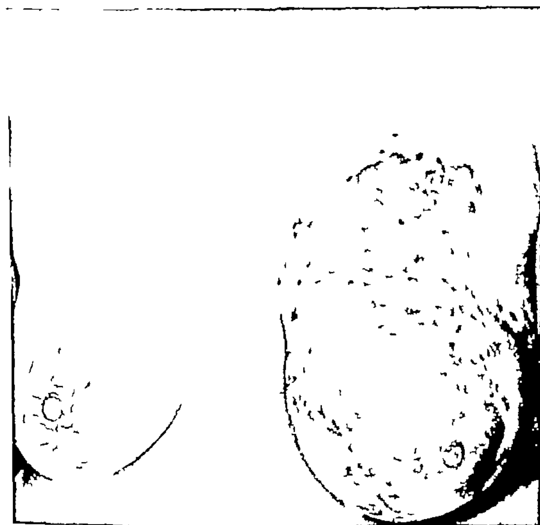


Fig 213 Sarcoid of the skin of the breast Appearance after three years

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lymph nodes Figure 214 shows the sarcoid in the mammary fat The carcinoma was of limited extent in the breast, and had not metastasized to the axillary nodes

After discharge from the hospital the patient's pulmonary symptoms increased She was given a course of cortisone as antisarcoid therapy

Three months after operation the patient developed an acute episode of abdominal pain for which she was readmitted as an emergency She was thought to have a dissecting aortic aneurysm

Treatment consisted of prophylactic digitalization, antibiotics and cortisone, and within the next two months she showed a definite improvement A chest rœntgenogram showed considerable decrease of the pulmonary shadows

She was readmitted for the third time seven months after operation, with another acute episode of pain involving the precordium and neck and expired soon after admission

Postmortem examination revealed the cause of the death to be a dissecting aneurysm of the aorta In addition sarcoidosis, involving the lungs, spleen, liver, lymph nodes, and tongue, was found

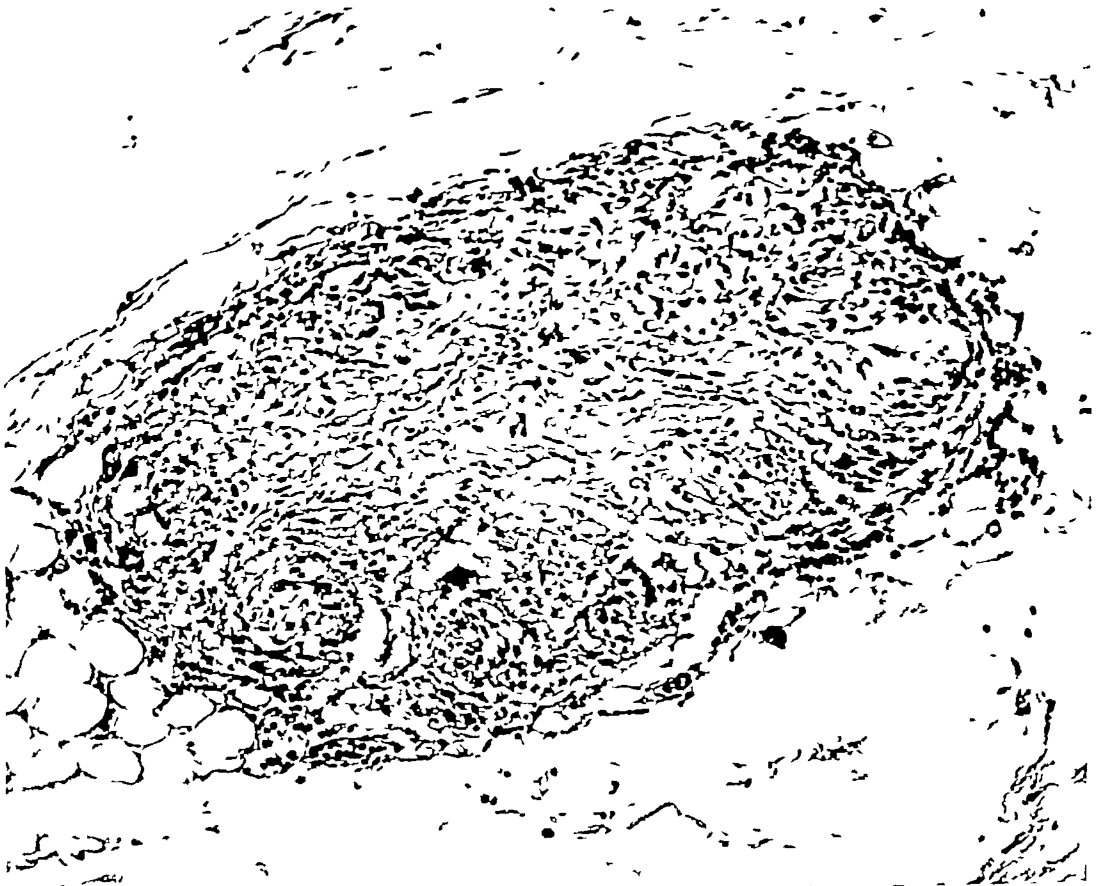


Fig 214 Microscopic appearance of sarcoid in the mammary fat

Syphilis of the Breast

Both primary chancre and secondary gumma are so rarely seen in the breast, even in large clinics for syphilis, that their clinical characteristics are not well defined The one feature of gumma that is common to most of the credible case reports is ulceration The best descriptions, with good illustrations, of both lesions have been published by Kampmeier

Reviews of previously reported cases of gumma of the breast, and descriptions of new cases have been published by Adair by Komori by Braunstein and Woolsey and by Whitaker and Moore A good many of the reported cases must be regarded as of a doubtful nature It is certainly impossible to differentiate gumma from other granulomatous processes on either clinical or microscopical grounds In our laboratory Lattes takes the sound position that the only proof of gumma is the regression of the lesion with antisyphilitic treatment We have no such acceptable case in our records

Rare Types of Infection in the Breast

Some of the very rare types of infection in the breast and the authors who have described them follow Filariasis (McFee) blastomycosis (Köhlmeier and Kreitner) sporotrichosis (Jung) leprosy (Furniss) scleroderma (Coleman)

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CHAPTER 17

THE ETIOLOGY OF BREAST CANCER

Carcinoma of the breast is one of the types of cancer concerning which a considerable amount of knowledge bearing on its causation has been accumulated We do not yet know its ultimate cause but we are perhaps closer to it than for any of the other major types of cancer

The Comparative Biology of Breast Carcinoma

As the century turned, Jensen of Copenhagen described mammary carcinoma occurring spontaneously in the mouse, and learned how to transplant it In 1903 he reported transplantation through 19 generations of mice over a period of two and a half years His experiments opened the modern epoch of experimental cancer research, and particularly, research concerning breast carcinoma

Mouse mammary carcinoma was at once seized upon as a means of studying cancer in general The research was carried on mainly in three laboratories, at the Pasteur Institute in Paris by Borrel, at Paul Ehrlich's new Institute for Experimental Therapy at Frankfurt a M , and in the London laboratories of the Imperial Cancer Research Fund Ehrlich was soon diverted from cancer research to the chemotherapeutic attack upon trypanosome disease Bashford and Murray, who organized the English laboratory in 1904, persevered and made it the first modern laboratory devoted exclusively to cancer research As such it was the forerunner of the many cancer research laboratories of today Bashford and Murray began with a study of animal tumors in general and went on to an intensive and prolonged investigation of the mouse tumors, including mouse mammary carcinoma The most important finding from this period of cancer research was that the disease is transplanted by living carcinoma cells They will live only in animals of the same species, and best in animals of the same strain Their growth characteristics do not change during countless transplantations and vicissitudes The mouse mammary carcinoma thus became the standard experimental tool of the modern cancer research worker, upon which he tests the effects of all types of therapeutic agents Provided that he transplants a mammary carcinoma of known character, using a careful standard technique, into a "pure" strain of mice, it is a remarkably reliable experimental tool

The value of mouse mammary carcinoma as an experimental tool has been greatly enhanced by careful selective brother to sister inbreeding Strains of mice have been developed in which the incidence of spontaneous mammary carcinoma is very high—as high as 95 per cent of the females developing the disease Simi-

larly strains of mice have been bred in which only a fraction of 1 per cent develop the disease. Maude Slye deserves the credit for this basic discovery the result of long years of patient work in her Chicago laboratory Many of these high and low mammary carcinoma strains of mice are now bred in laboratories all over the world Even after hundreds of generations of selective breeding they cannot be said to be genetically pure and will revert toward a common type unless the selective breeding is continued

From the study of mammalian pathology it has become known that mammary carcinoma occurs in only a few species of wild or domesticated mammals It is seen rarely in rats and rabbits It is frequent only in mice and dogs, species which it must be pointed out live in association with man the only other mammal afflicted with the disease

The general characteristics of mammary carcinoma are so similar in the mouse the dog, and in man that it is very likely that the etiology of the disease is the same in all three species To begin with, the natural history of the disease, its localized origin from the mammary epithelium its regional spread and its metastases, are similar in all three species although the disease evolves more slowly and is less likely to metastasize and can therefore be said to be less malignant in the dog and the mouse than in man Histologically the disease has similar basic histological features in all three species It is true that special forms of epithelial metaplasia—squamous metaplasia cartilaginous metaplasia and sarcomatoid metaplasia—occasionally seen in mouse carcinomas and frequently seen in the dog carcinomas are a rare phenomenon in human carcinoma of the breast. Finally recent studies of the hormonal relationships of mammary carcinoma have shown that in both the mouse and in man these are similarly influenced by the steroid hormones

The Steroid Hormones and the Etiology of Breast Carcinoma

It is well known that the physiology of the mammary gland is controlled by the ovarian adrenal and pituitary hormones This fact led investigators to study the relationships of these steroid hormones to the development of mammary carcinoma Here again the mouse has been the main experimental subject. Cori was the first in 1927 to show that the removal of the ovaries in very young female mice of high carcinoma strains entirely prevents the development of mammary carcinoma No one has succeeded in removing the pituitary or adrenals in these small animals and keeping them alive so that we do not know that these glands are equally necessary for the development of mammary carcinoma.

There is suggestive evidence that the incidence of mammary carcinoma is lower in women who have had bilateral oophorectomy Herrell in the Mayo Clinic data, found that only 1 5 per cent of women with breast carcinoma had had their ovaries removed earlier in life, while 15 4 per cent of a control series of women not having breast carcinoma had had bilateral oophorectomy Dargent has also published some data bearing on this question but it needs further study in better controlled clinical material

Ovarian function as manifested by the menstrual history has been investigated in several series of patients with breast carcinoma Lane Claypon studied the duration of menstrual life and found it to be slightly longer in her series of

233 patients with breast cancer than in her control series B and P Heiberg reviewed the menstrual histories in a series of 517 Danish women with breast carcinoma and concluded that the menopause occurred later in this group than in normal women Olch reached a similar conclusion from a review of the case histories of 342 women with breast cancer Smithers reported the mean total duration of menstrual life in a series of 290 women with breast cancer to be 34 6 years, which is significantly longer than that of Lane-Claypon's breast cancer series as well as Lane-Claypon's control series

Another method of studying the etiological role of hormones in mammary carcinoma is, of course, to administer them to mice Lacassagne was the first in 1933 to treat mice with estrogen He believed that he had induced mammary carcinoma Subsequent studies (Haagensen and Randall) showed that excessive and prolonged estrogen treatment of female mice does not modify the tendency to develop the disease inherent in the strain, except to produce it at an earlier age in the high mammary carcinoma strain mice The mean age at which our RIII bred females developed the disease was 12 1 months, while estrogen treated females developed it at a mean age of 8 1 months Estrogen did not induce the disease in females of our low mammary carcinoma C57 strain Estrogen does, however, produce mammary carcinoma in male mice of high mammary carcinoma strains, presumably by stimulating the growth of a female type of breast in the males In this sense only did Lacassagne induce mammary carcinoma The inherited genetic strain predisposition, or some extrachromosomal factor transmitted from one generation to the next, is dominant over the estrogenic effect

In human beings there is likewise no proof that the administration of estrogen —now so generally given to women for a great variety of symptoms—induces mammary carcinoma There have been striking cases, such as the one described by Auchincloss and myself, in which the long continued administration of estrogen preceded carcinoma of the breast, and in which pathological study showed, in addition to the carcinoma, a great variety of types of epithelial proliferation in both breasts The epithelial proliferation in such a case is almost certainly the result of the intense estrogen stimulation, but we are not justified in assuming that the carcinoma also was induced by the estrogen We might transpose to women what we have learned from the mice and conclude that estrogen will cause carcinoma of the breast to appear prematurely in women destined by their genetic constitution or by an extrachromosomal factor to develop the disease This fact in itself should be sufficient to make physicians hesitate to administer estrogen Certainly it should not be given to women who have a family history of breast carcinoma

The question of whether or not estrogen induces carcinoma of the breast in men is a controversial one Since the breasts of patients with prostatic cancer who have been treated with estrogen regularly show proliferative changes, it might be expected that these changes would in some instances give rise to mammary carcinoma A series of cases have in fact been reported in which this sequence is assumed to have occurred (Keller, Gibba, Jakobsen, Graves and Harris, Claisse and Daymas, McClure and Higgins, Corbett and Abrams, Howard and Grosjean, Reimann-Hunziker, Gardini, Abramson and Warshawsky)

It is unfortunately a fact that carcinoma of the prostate is similar histologically to some forms of carcinoma of the breast and that it is difficult at times to distinguish the metastases of prostatic carcinoma to the breast from primary breast carcinoma. Campbell and Cummins have described a case in which they interpret the breast lesions as metastatic and they suggest that previously reported cases of presumed breast carcinoma developing during stilbestrol therapy are also examples of metastases of the prostatic carcinoma to the breast

This question cannot, perhaps, be finally decided as yet, but the evidence seems very strong that at least in some of these cases the breast lesions were genuine primary mammary carcinomas For instance, in a case reported by Baierl, the patient did not have prostatic cancer He was treated with stilbestrol for a gastric ulcer and developed a breast carcinoma for which radical mastectomy was done. He remained well a year after operation In some of the patients with prostatic carcinomas who have developed breast lesions while taking stilbestrol there were no distant soft tissue metastases of the prostatic carcinoma at the time the lesion was removed surgically or at the latest follow up some time later (as in the case of Graves and Harris) It would seem unlikely that isolated metastasis of prostatic carcinoma to the breast would occur in the absence of other distant soft tissue metastases.

Still another type of hormonal effect in mice is that caused by the administration of androgen If given in large doses over a prolonged period of time to young female mice of high mammary carcinoma strains androgen will prevent the development of mammary carcinoma This effect is the result, we may assume, of the suppression of ovarian function by the overwhelming dosage of androgen

The Genetic Inheritance of Breast Carcinoma

Although mammary carcinoma is certainly inherited we do not know how The availability of relatively homogeneous high and low mammary carcinoma strains of mice has made it possible to carry out elaborate genetic studies in which the results of cross-breeding upon the incidence of the disease have been observed for many generations. There is as yet no general agreement as to genetic type of inheritance Slye originally thought that the mammary carcinoma was inherited as a Mendelian recessive but Lynch concluded it was a Mendelian dominant Dobrovolskaia Zavadskaia had a more complex explanation Since the discovery of an extrachromosomal milk factor which I shall discuss presently the complexity of the problem of the mechanism of the inheritance of mammary carcinoma has greatly increased.

In human beings the familial inheritance of breast carcinoma has been emphasized in reports, dating back almost a hundred years of noteworthy family pedigrees. Jacobsen reviewed these early reports in his monograph Heredity in Breast Cancer " the most comprehensive study of the question yet to appear One of the earliest of these pedigrees of cancer families was that published in 1866 by the distinguished French clinician Broca of his own family He traced the cause of death for all the 38 members in five generations of his family dying between 1768 and 1856 One of the 14 men and 15 of the 24 women died of cancer and 10 of the women had cancer of the breast The family history type of inquiry was carried out in great detail in our own country by Warthin

During the last twenty-five years a series of statistical studies of the heredity of breast cancer from Norway, Holland, Denmark, England and our own country have provided us with a much more broadly based kind of evidence

Waaler's Norwegian study (1932) consisted of an investigation of the causes of death in relatives of some 6000 cancer patients, and a comparison of these data with the mortality for cancer in the Norwegian population as a whole He found that the incidence of cancer of the breast was much greater among sisters of patients with this disease than it was among sisters of patients with cancer but not of the breast

Wainwright in 1931 reported a study of the frequency of cancer in the parents, brothers and sisters of 784 women treated for breast carcinoma He used 576 well females between the ages of 45 and 70 as controls Breast carcinoma was four times as frequent in the mothers of his breast carcinoma patients as in the mothers of the controls Wainwright's study, although representing a great personal effort, was not adequately controlled

Wassink, in 1935, presented the results of an extensive investigation of the frequency of cancer in the parents, brothers and sisters, grandparents, and first cousins, of 660 Dutch women with mammary carcinoma These 660 women had a total of 301 relatives with cancer of all sites, of whom 192 were females and only 109 males One hundred and twelve, or 58 per cent of the 192 female relatives, had breast carcinoma This finding represents a marked increase in breast cancer in the female relatives of the women with breast cancer In the Dutch female population as a whole mammary cancer forms only 10 or 12 per cent of cancers of all sites in females

Jacobsen, in his 1946 monograph "Heredity in Breast Cancer," described a detailed genealogical study of the families of 200 women with breast cancer treated in Copenhagen hospitals His investigations included grandparents, parents, uncles and aunts, and brothers and sisters Among the female relatives there were 71 cases of breast cancer, representing 35 per cent of the cancers developing in all sites In Jacobsen's control series of the families of 200 women not having cancer, only 8 cases of breast cancer were found, representing only 18 6 per cent of all the cancers developing in all sites Jacobsen's calculation showed the difference in the incidence of breast cancer in the two groups of women to be three times the standard error of the difference and he concluded that it is "overwhelmingly probable that the development of cancer of the breast is due to hereditary predisposition " Jacobsen's data were subsequently studied and re-computed by Busk, Clemmesen, and Nielsen, and his main thesis confirmed Busk also demonstrated that when a woman has a cancer of the right breast, her mother and sisters are predisposed not only to develop the disease but to develop it in the right rather than the left breast

Smithers, in 1948, reported an investigation of the family histories of 459 patients with carcinoma of the breast treated at the Royal Cancer Hospital of London He found that 76 of the patients had a family history of breast carcinoma this group constituted 45 5 per cent of the total of 167 patients with a family history of cancer in all sites Smithers concluded that his breast cancer patients had a significantly high family history of breast cancer

Penrose and his associates, in 1949, described their findings in tracing the

frequency of deaths from cancer in the families of a series of 510 women with breast cancer treated at the University College Hospital or the London Hospital. Forty nine deaths from mammary cancer were verified in these families On the basis of calculations from mortality data for England and Wales only 18 19 deaths from breast cancer were to be expected Penrose concluded that mammary cancer occurs with a significantly increased frequency in the mothers and sisters of patients with this disease.

The data from my personal case history files regarding familial cancer history are summarized in the following table

Table 27 Familial History of Cancer in Personal Cases of Breast Carcinoma

Total number of patients	419
Total reporting family history	403
Number of patients with cancer in family	152, or 37 7% of those reporting history
Total number of relatives with cancer	228 or 60 males and 168 females
Number of patients with breast cancer in family	69 or 17 1% of all reporting history and 45 4% of those with family history of cancer
Total number of relatives with breast cancer	86 or 51.2% of all female relatives with cancer
Number of mothers with breast cancer	21 or 5.2% of all mothers of patients who reported family history
Number of sisters of patients with breast cancer	21

The impressive evidence from these genealogical studies that mammary carcinoma is inherited finds further support in the simultaneous and symmetrical occurrence of the disease in homologous twins a number of examples of which have been reported by Burkard, by McFarland and Meade, by Munford and Linder by Phillips, by Weitz, by Habs by Kranz, and by Busk Clemmesen and Nielsen

The Extrachromosomal Inheritance of Mammary Carcinoma

In 1936 Bittner made the remarkable discovery that in mice the development of mammary carcinoma is dependent upon a factor transmitted by the mother in her milk to her offspring Mice from a low mammary carcinoma strain foster nursed by a mother of a high mammary carcinoma strain developed the disease with a high frequency The converse was equally true foster nursing of high mammary carcinoma strain mice by mothers belonging to low mammary carcinoma strain markedly diminished the frequency of the disease in them Bittner concluded from his discovery which was soon confirmed in other laboratories that an extrachromosomal factor present in the milk played an important part in the transmission of mammary carcinoma.

The next and obvious step was to identify isolate, and characterize this factor At Columbia University a team of chemists, physicists and biologists began work on the problem soon after Bittner s discovery and has been actively working upon it ever since At the National Cancer Institute Andervont and his associates have carried out extensive investigations of the milk factor over a period of years Another group at the University of Leeds, including Passey Astbury and Dmochowski has worked at the problem Bittner and his associates at the University of Minnesota have of course continued their studies

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research has been analyzed by Korteweg He points out that if the extrachromosomal factor is transmitted by milk it must be through the maternal not through the paternal line. In Jacobsen s data there were 50 family pedigrees in which there was more than one case of breast cancer The transmission was through the maternal line in 42 and through the paternal line in only 14 In Smithers data there was a maternal family history in 100 cases and a paternal family history in 46 The ratio of two to one in favor of an inherited maternal influence might seem to indicate the existence of an extrachromosomal milk factor Korteweg points out however that a preponderance of the maternal over the paternal line is to be expected because of the simple fact that the average number of members per family in the data is three On the average, the mother s family consisted of her self and a brother and a sister that is two women and one man Korteweg therefore finds no support for the concept of an extrachromosomal milk factor in human mammary carcinoma

The Relationship of the Development of Mammary Carcinoma to Mammary Function

In some strains of mice the incidence of mammary carcinoma is slightly lower in unbred females in whom the mammary glands never of course, function In our RIII strain of mice, for example, the incidence of the disease in unbred mice is diminished by approximately one third. This relationship between breeding and the incidence of mammary carcinoma varies however among different strains of mice

Bagg showed that the interference with the normal mammary gland function in mice which occurs when the newly born litters are removed from the mother and she is at once again bred increases the incidence of mammary carcinoma in mice of low mammary carcinoma strains.

In women there is abundant evidence that carcinoma of the breast is more frequent in individuals whose breasts have not functioned normally Gilliam studied the marriage and pregnancy records of 849 hospital patients with breast cancer and found that they had fewer pregnancies and also fewer live births than women in the general population In two recent large English series of cases (Hartnett s 2,129 cases and Smithers 1 762 cases) approximately 22 per cent of the patients were unmarried This is significantly higher than the expected figure of 17 per cent of unmarried women in the general English population In our Presbyterian Hospital data for the years 1935–1942, 23 3 per cent of the native white women admitted with breast carcinoma were single, as compared with an expected percentage of 15 3 calculated from the proportions found by the census of 1940 for native white women in U S cities with a population of 250 000 or more

Norwegian data concerning 1,584 women with breast cancer recently published by Rennaes and Holan confirm the greater frequency of the disease in unmarried as compared with married women, and also the great diminution of the frequency of the disease as the number of children increases. Their age incidence charts of these different groups of women with breast carcinoma are so striking that I have reproduced them here (Charts 9 and 10)

Denoix and Moine, in 1951 reported French mortality data for mammary

Many things have been learned about the milk factor It is present in the mammary carcinoma tissue itself, as well as the mouse tissues in general, and in blood, although only in a very limited amount By far the best source of the factor, however, is mouse milk, and to provide experimental material for our research effort at Columbia we have maintained a large mouse dairy Andervont has recently proved that the factor is present in semen and that it can be transmitted in this medium from male to female

In experimental work the factor, whether obtained from milk or from tumor tissue, is ordinarily injected intraperitoneally into test animals of a known low mammary carcinoma strain A remarkable feature of the milk factor is its long latent period, for if the experimental induction of the disease is to be successful mice no more than two, or at the most three, weeks of age must be used Mammary carcinoma then develops at a mature age for the mouse, at a mean of approximately twelve months

The milk factor is easily killed by heat, but it withstands freezing and drying well It must be a very small particle, in the order of 20 to 100 millimicrons, for we have induced mammary carcinoma with it in dilutions as high as 10^{-12}

Beyond these basic facts we have not yet succeeded in characterizing the milk factor Our chief analytical tools, the electrophoresis apparatus, the ultracentrifuge, and the electron microscope, have not enabled us to identify it Earlier in the course of our own studies we believed that we had visualized the factor in the electron microscope We now know that the particulate matter that we see in the electron microscope cannot, for the moment, be surely identified

Very little has as yet been done in investigating the extrachromosomal factor in human beings Our team of workers feel that it is unwise to attempt to identify the factor in human milk until we have succeeded in identifying it in mouse milk Mouse mammary carcinoma is an almost perfectly controlled experimental tool, and it seems reasonable to concentrate our efforts upon it for the present Reports such as that of Gross, claiming to have visualized a virus-like milk factor in human milk, cannot be regarded seriously

There is as yet very little direct historical evidence that there is an extrachromosomal factor in the inheritance of mammary carcinoma in women Wood and Darling described a remarkable family in which the occurrence of numerous breast carcinomas in four generations had a suggestive relationship to the nursing history I have carefully taken nursing histories on my patients with breast carcinoma ever since Bittner's discovery, and I am convinced that such histories are entirely unreliable The milk factor, if it does exist in human beings, is certainly such a small particle that putting an infant to breast even once would be enough to transmit it We have induced mammary carcinoma in mice by feeding one drop of milk to a young mouse We need to know that the individual in question was never put to breast even once Patients do not know such details of their infancy They often are ignorant of whether or not they were nursed in the conventional sense of the word A long range inquiry on the influence of nursing in the subsequent lives of present day infants is being carried out at the University of Minnesota but it will be at least fifty years before their data can begin to have any meaning

The indirect evidence of an extrachromosomal milk factor from genealogical

are shown in Table 28 In Japan (Chart 12) the death rate from breast carcinoma is only about one-sixth of that in the United States, according to Dorn

Table 28. Percentage of All Cancer Reported Among Women—1949

Site	*Puerto Rico*	New York State (exclusive of New York City)
Breast	9 1	22 1
Cervix	35 1	10 3

Social traditions that Puerto Rico and Japan with a low mammary carcinoma rate have in common are early marriage, a high birth rate, and the custom of breast feeding *It seems likely that differences in the incidence of breast carcinoma* are more closely related to differences in breast function than to inherited racial differences, that is, to genetic constitution

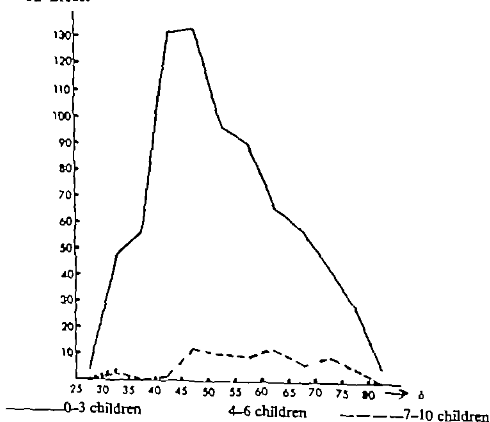


Chart 10 The age distribution of 1,049 women with carcinoma of the breast according to parity (Rennaes and Holan)

There is unfortunately very little direct statistical evidence as to the relation ship between breast function and the subsequent development of cancer in terms of the number of children breast fed and the length of time they were nursed Lane Claypon, in her 1926 study reported a careful inquiry into the lactation history of 213 mothers with breast cancer as well as a control series of 245

carcinoma which also showed that the disease is more frequent in nulliparous women than in women with children, and that its incidence diminishes as the number of children increases

Clemmesen's Danish Cancer Registry morbidity data for breast cancer in Denmark are the most inclusive yet available They show that the disease is considerably more frequent in unmarried than in married women

One of the most interesting contributions regarding carcinoma of the breast is the study of Indian women by Khanolkar Indians are sharply divided by the caste system into groups with different economic and social traditions and customs The Parsees are a small, well knit group with close interbreeding They

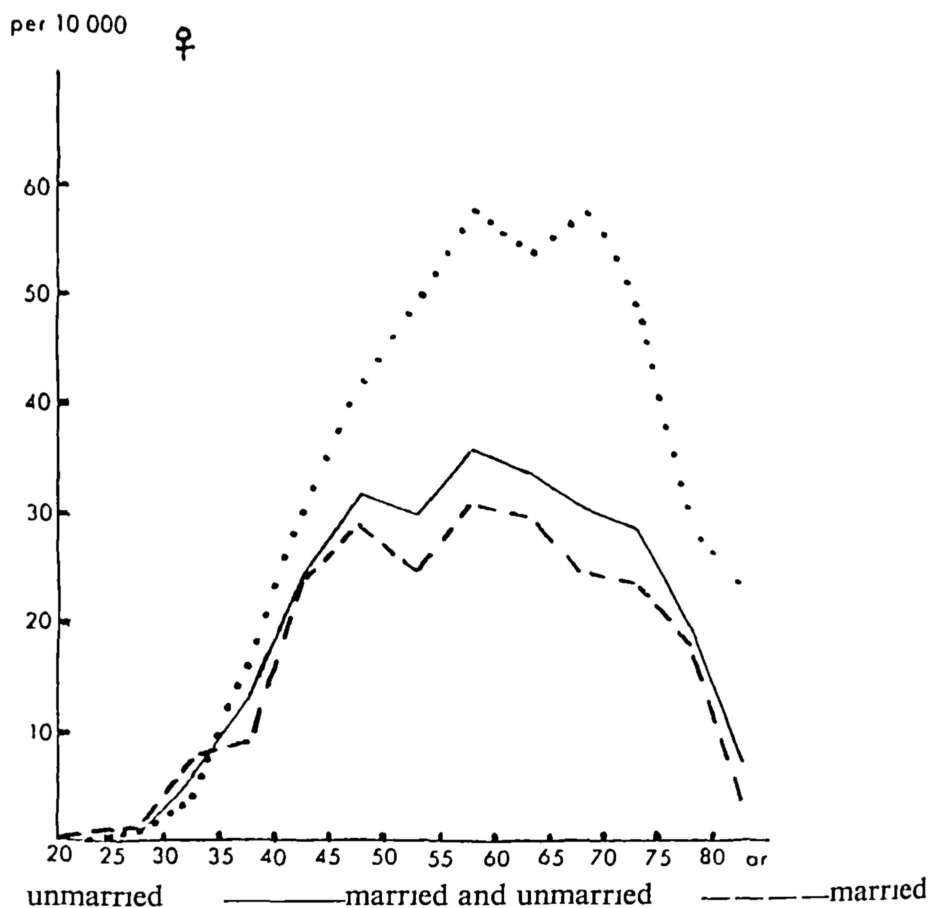


Chart 9 The age distribution of 1,049 married women and 499 unmarried women with carcinoma of the breast (Rennaes and Holan)

are well to do, marry late, at an average age of 25, and have few children which they often do not nurse They have high incidence of mammary carcinoma Hindu women, who are poor, marry early, at an average age of 16, and have numerous children whom they usually nurse, have a much lower incidence of mammary carcinoma These findings are strikingly shown in Khanolkar's chart of the frequency of carcinoma in his patients at the Tata Memorial Hospital (Chart 11)

There are a number of regions with comparatively reliable vital statistics, such as Puerto Rico and Japan, that show a much lower breast carcinoma rate than is found in modern European countries and in the United States Comparative frequencies for breast and cervical cancer in Puerto Rico and in New York State

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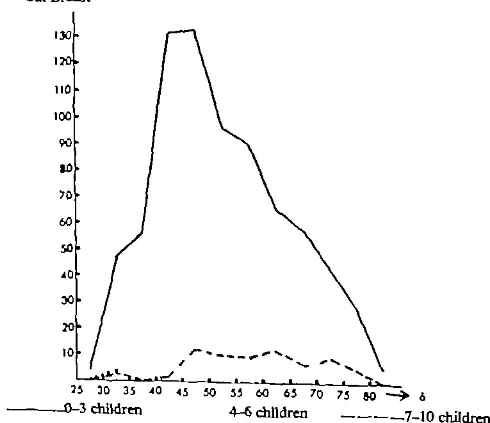


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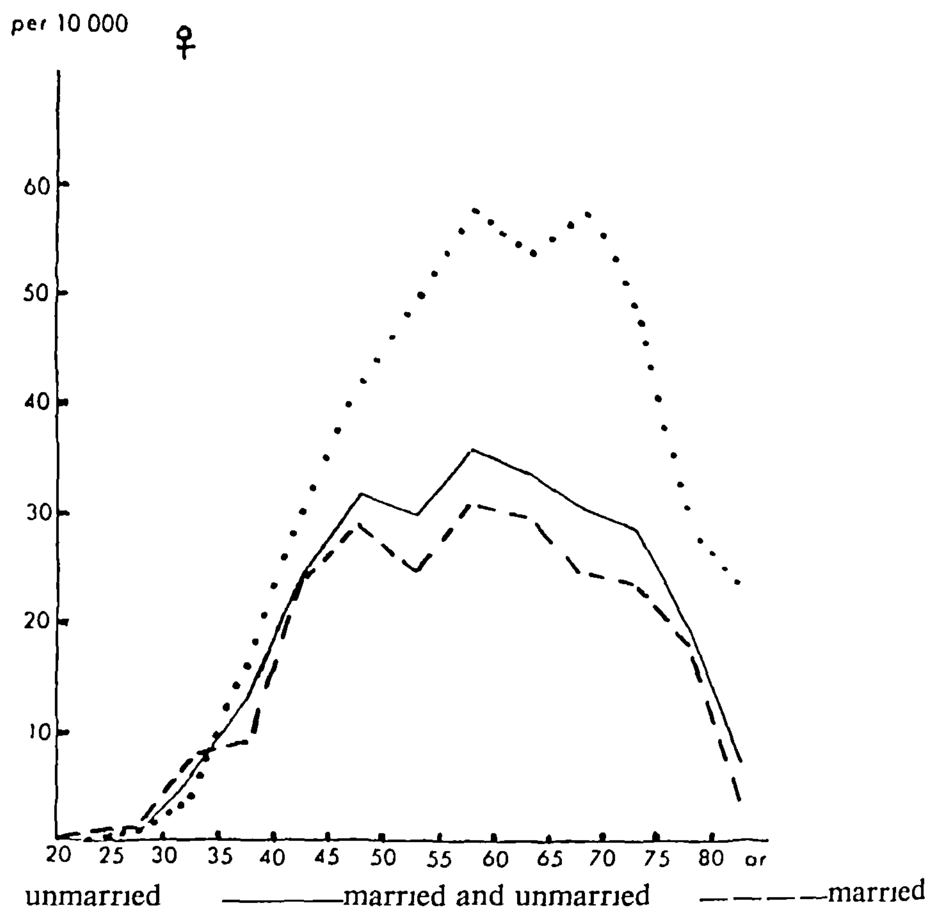


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I have always attempted to take exact nursing histories of this kind in the patients with breast carcinoma whom I have seen but I lack truly comparable control data regarding the extent to which women from the same social class and age groups who did not have breast cancer have nursed their children A great change in infant feeding has occurred in our country recently Fifty years ago the overwhelming majority of American women nursed their children Today deterred by both obstetricians and pediatricians very few women breast feed their babies Almost 30 per cent of the children of my patients with breast

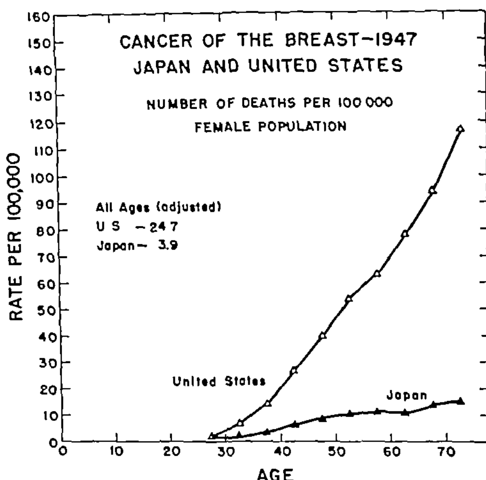


Chart 12. The incidence of cancer of the breast in Japan and the United States (according to Dorn)

carcinoma have not been breast fed—a figure twice as high as Lane-Claypon s English percentage of 25 years ago This abandonment of breast feeding is today common to women of all social strata seen in an urban hospital It is rare today at least for me to find a middle aged patient who has successfully breast fed a number of children. This simple fact may be of fundamental importance in the modern high frequency of mammary carcinoma

A summary of the lactation records of my own personal patients is given in Table 29 with comparative figures from the Lane-Claypon and Smithers series.

Unfortunately there are no control series figures for the percentage of parous

mothers who did not have cancer She found that 14 6 per cent of the children of the mothers in the cancer series had never been breast-fed, as against 7 4 per cent in the control series Smithers recalculated her results, including stillbirths and correcting the cancer series to the same family size distribution as the con-

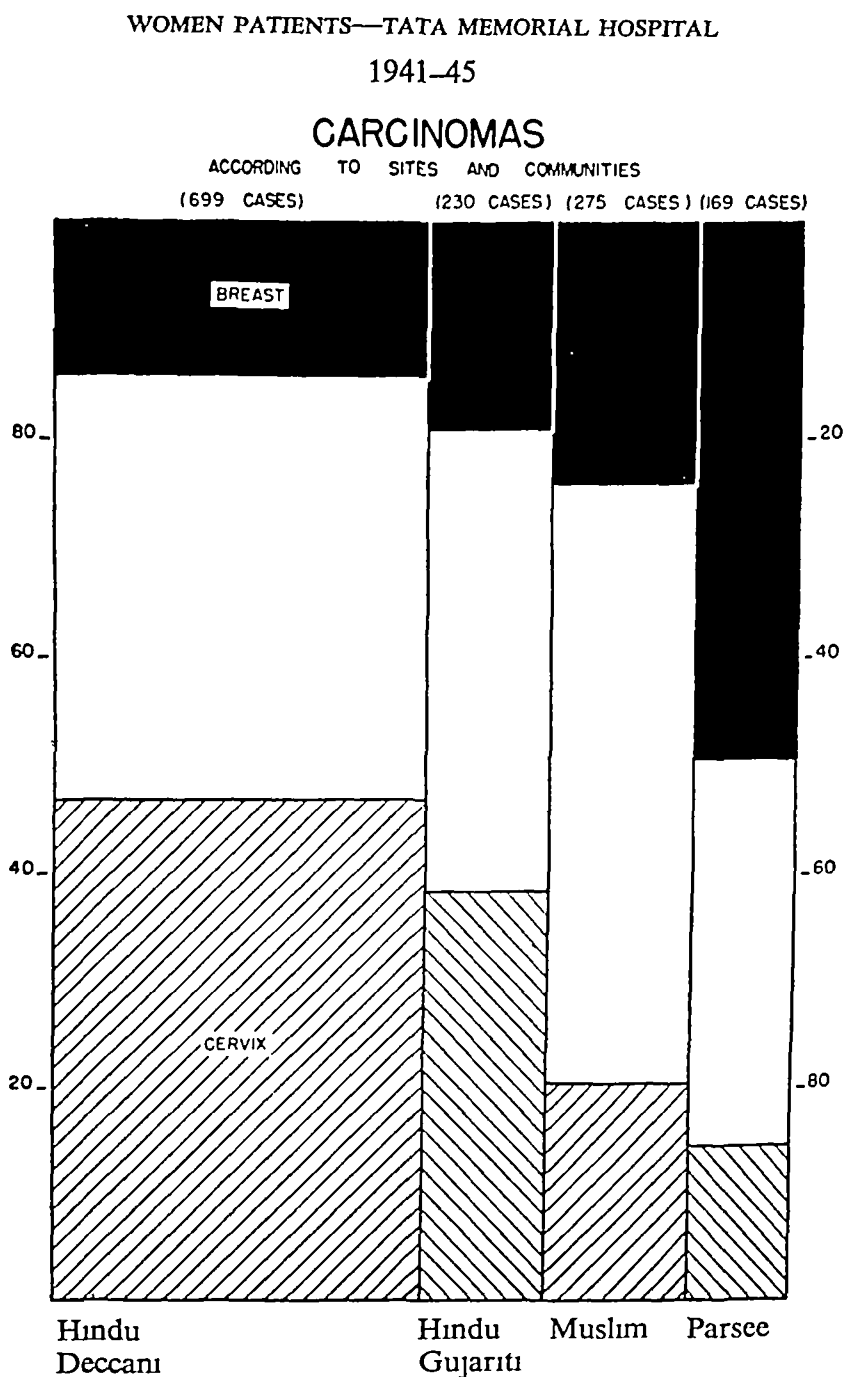


Chart 11 The incidence of carcinoma of the breast in different Indian castes (according to Khanolkar)

trols, and the difference between the two series was still nearly 7 per cent His own study of the lactation histories of 321 mothers with breast cancer in the Royal Cancer Hospital gave a figure of 18 63 as the percentage of children not breast-fed

The parity distribution to be expected in a normal group of women of this size can be found by applying the proportions shown in the census data of the totals of each age group When both the actual and the expected parity distributions in our series of patients with breast cancer are summed up and compared the results are not dissimilar to those found by Stocks in his analysis of data from the Royal Cancer Hospital. The proportion of women with fewer than the expected number of children was abnormally large in both our Presbyterian and in the Royal Cancer Hospital patients with breast cancer Table 31 shows both distributions for ages over 45 and the ratio for all ages.

Table 31. Native White Women with Breast Cancer—Actual and Expected Parity Distributions

Number of children	*Presbyterian Hospital* Women aged 45 and over				*Royal Cancer Hospital* Women aged 45 and over			
	Actual number	Expected number	Ratio	Ratio for all ages	Actual number	Expected number	Ratio	Ratio for all ages
0	40	33 4	1 20	1 19	50	40 4	1 24	1 27
1	44	30 1	1 46	1 25	72	57 4	1 25	1 20
2	37	31 7	1 17	1 15	65	65 3	1 00	1 09
3	15	21 8	69	78	47	47 9	98	95
4	11	13 1	84	84	23	31 5	73	60
5 or more	5	21 9	23	30	46	60 5	76	64

The Relationship of Inflammation and Trauma of the Breast to the Development of Mammary Carcinoma

Lane-Claypon made a careful study of the relationship of puerperal mastitis, non suppurative as well as suppurative to the development of cancer of the breast, and found no evidence that these lesions predisposed to cancer

In any series of cases of breast cancer many instances will be found of the patient attributing her carcinoma to antecedent trauma to the breast. In her 1926 series of cases Lane-Claypon had a strikingly high percentage (26 8 per cent) of patients who claimed antecedent breast injury Since cancer is somewhat more common in the left than in the right breast Lane-Claypon who believed that trauma does predispose to breast cancer suggested that this left-sided predominance is due to the fact that right handed persons protect the right breast from being traumatized

From my own experience with mammary carcinoma I doubt that trauma is a factor in its causation It is the most natural thing in the world for a scientifically uncritical patient to attribute any and all disease to trauma. Most patients with breast cancer whose case histories have provided the data for reports such as Lane-Claypon s are uneducated ward patients, prone to prejudice and suggestion The leading question regarding antecedent trauma put to them by the intern taking the history no doubt often suggests this easy explanation for their disease to them In the case histories of breast carcinoma that I have myself taken it has been a rare thing for the patient to give a definite and precise story of antecedent breast trauma

women who nursed no children at all It would be interesting to know whether this group is conspicuously larger among patients with cancer than in the populations from which they came In our own series of breast cancer patients some 25

Table 29. The Relationship of Breast Feeding to Carcinoma of the Breast

	Control series	Cancer series		
	Lane-Claypon	Lane-Claypon	Smithers	Haagensen
Number of women in sample	509	508	483	419
Number who bore living children	245	213	321	268
Per cent who bore living children	48 1%	41 9%	66.5%	64 0%
Total number of children	1342	875	887	659
Average number children per mother	5 5	4 1	2 7	2.5
Number children with known nursing history	1337	869	864	641
Number children not breast-fed	99	127	161	185
Per cent of children not breast-fed	7.4%	14 6%	18.6%	28 9%

per cent reported that none of their children were nursed as against 14 per cent in Smithers' series from the Royal Cancer Hospital

When parity only is considered we are somewhat better off for control figures because the U S Census of 1940 Studies make it possible to calculate parity distribution for native white women residing in cities of 250,000 inhabitants or

Table 30 Number of Native White Women Who Had Borne Given Number of Children at Onset of Breast Carcinoma, By Age
(Presbyterian Hospital 1935–1942)

Number of children	Age of mother							Total
	30–34	35–39	40–44	45–49	50–54	55–64	65–74	
0	3	10	7	8	5	14	13	60
1	3	6	7	15	11	12	6	60
2	3	6	10	6	8	14	9	56
3	2	1	6	2	3	6	4	24
4	—	1	3	—	3	5	3	15
5 or more	—	1	2	—	4	—	1	8
Total	11	25	35	31	34	51	36	223

more by age groups between 30 and 75 Three hundred and forty-eight of the 668 patients who came to the Presbyterian Hospital with breast cancer between 1935 and 1942 fall into this class, 267 were married, and 223 of these reported the number of their children The parity distribution of these women is shown in Table 30

The parity distribution to be expected in a normal group of women of this size can be found by applying the proportions shown in the census data of the totals of each age group When both the actual and the expected parity distributions in our series of patients with breast cancer are summed up and compared the results are not dissimilar to those found by Stocks in his analysis of data from the Royal Cancer Hospital The proportion of women with fewer than the expected number of children was abnormally large in both our Presbyterian and in the Royal Cancer Hospital patients with breast cancer Table 31 shows both distributions for ages over 45 and the ratio for all ages

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The Relationship of Benign Tumors of the Breast to Mammary Carcinoma

The most debated of all questions regarding the etiology of mammary carcinoma is its relationship to the various benign tumors of the breast, adenofibroma, cystic disease, intraductal papilloma, etc The problem has recently been discussed by Charteris, Dawson, Ducuing et al , and Lewison and Lyons I have dealt with this question in relation to each of the various benign lesions separately, in the chapters devoted to them There is no need of repeating my point of view

I can summarize, however, my own experience, and that of my mentor, Dr Stout, by stating that we do not regard as precancerous any of the benign lesions of the breast that I have described, with the single exception of cystic disease And the fact that women with clinically evident cystic disease develop mammary carcinoma approximately four times as frequently as women in the general population does not justify bilateral prophylactic mastectomy, the only therapeutic procedure that would protect them They, like the women whose familial inheritance predisposes them to an equal degree to mammary carcinoma, should examine their own breasts or have them examined by a physician, at least every three months This is the practical conclusion to which our modern knowledge of the etiology of breast cancer leads us

The Relationship of Non-Cancerous Disease in Organs Other than the Breast to Mammary Carcinoma

Studies of the possible relationship of carcinoma of the breast to a wide variety of non-cancerous lesions of organs other than the breast have been made, without finding any statistically significant correlation Some of the lesions that have been investigated follow pituitary adenoma (Steiner and Dunham), adrenal adenoma (Flynn and Halliday), granulosa cell tumor of ovary (Finkler), thyroid disease (Moehlig, Repert), diabetes (Repert), acanthosis nigricans (Curth)

The Relationship of Cancer of Organs Other than the Breast to Mammary Carcinoma

The question of the association of malignant disease in the breast with that in other organs has been intensively studied (Curran and Kilroy, Englebreth-Holm, Huber, Larson and Kunz, Leidinger, Mider et al , Wassink)

These studies have not revealed a statistically significant association of breast carcinoma with cancers of other organs, except possibly with ovarian and uterine cancer Uterine carcinoma is certainly associated with breast carcinoma more often than any other type

In our Presbyterian Hospital cases of carcinoma of the breast seen between the years 1935 and 1942, a period during which our case histories have been more complete, previous or subsequent malignant disease in other sites was observed as shown in Table 32

There are certainly basic and as yet unknown factors concerned in the causation of both breast cancer and cancer of the cervix by which both are related to the married state While marriage tends to diminish the number of breast cancers

Table 32. Cancer of Other Sites Reported in 668 Patients with Breast Carcinoma
(Presbyterian Hospital 1935–1942)

Cervix and corpus	7
Ovary	2
Colon and rectum	4
Stomach	1
Pancreas	1
Bladder	2
Bronchus	1
Tonsil	1
Thyroid	1
Skin	2 (1 epithelioma) (1 malignant melanoma)
Lymphosarcoma	1
Total number of patients	23 or 3 4/

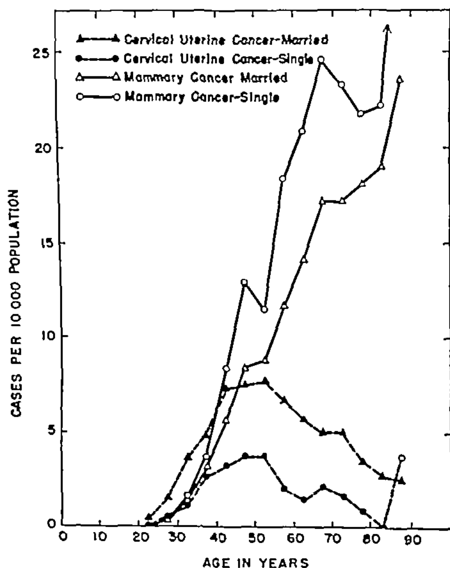


Chart 13 The incidence of uterine and mammary cancer (after Clemmesen)

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Bladder	2
Bronchus	1
Tonsil	1
Thyroid	1
Skin	2 (1 epithelioma) (1 malignant melanoma)
Lymphosarcoma	1
Total number of patients	23 or 3.4%

CERVICAL UTERINE AND MAMMARY CANCER
MORBIDITY RATES BY AGE AND MARITAL STATUS
DENMARK 1943–47 (THE DANISH CANCER REGISTER)

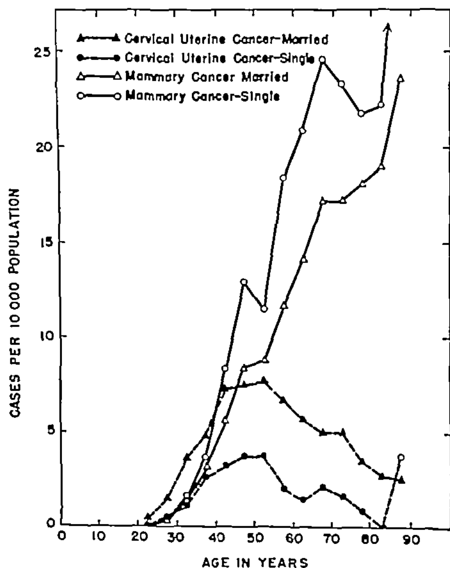


Chart 13 The incidence of uterine and mammary cancer (after Clemmesen)

it increases the number of cervix cancers And it is now apparent in the data from a number of countries that the incidence of breast cancer rises as the incidence of cancer of the cervix falls, and vice versa Clemmesen, whose data are shown in Chart 13, has done more than any other modern student to establish these facts He has pointed out that this observation was first made a hundred years ago by Stern in Italy Detailed studies such as that of Gilliam, using age of marriage, length of married life, total number of pregnancies and other relevant data, will be necessary before the real relationships between marriage and cancer of the breast and cervix can be established

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CHAPTER 18

THE FREQUENCY AND AGE DISTRIBUTION OF MAMMARY CARCINOMA

An appreciation of the true frequency of a disease is basic in the attack upon it. Our impression of the frequency of mammary carcinoma has, in the past, been based chiefly upon mortality data. Within recent years reliable morbidity data have become available that give us a more accurate picture of the frequency of the disease

Frequency

Mammary carcinoma is one of the great diseases In this country it is respon sible for the deaths of some 17 000 women annually The mortality rate for the

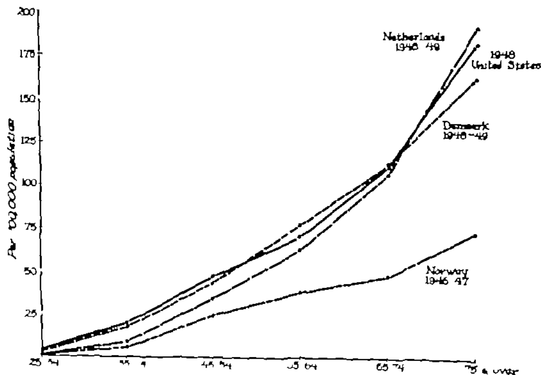


Chart 14 The mortality from cancer of the breast by age.

disease in western European countries with reliable vital statistics approximates that of this country as shown in Chart 14

The mortality of mammary carcinoma in this country compared with that of some of the other great diseases is shown in Chart 15

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The age distribution of our Presbyterian Hospital patients with breast carcinoma during the years 1915–42 is shown in Chart 16

Morbidity data from Denmark France, and the states of New York and Connecticut are plotted in Chart 17 These are of course relative data and represent the annual frequency of mammary carcinoma in the total female population within each quinquennial age group From this chart it will be seen that the incidence of mammary carcinoma in Denmark climbs sharply after the age of 35 and reaches one peak between the ages of 45 and 50 The incidence of the disease

Table 33. Selected Cancer Incidence Rates Per 100 000 Males or Females
(Annual Average for All Ages)

	Denmark 1943–1947		New York State 1945–1947		New York State 1949–1951	
Males	1 Stomach	45.3	1 Skin	30.9	1 Skin	37.4
	2 Rectum	21.0	2 Prostate	24.6	2 Prostate	28.4
	3 Skin	18.4	3 Stomach	23.0	3 Lung and bronchus	27.4
	4 Colon (incl.)	15.8	4 Colon	19.2	4 Stomach	23.8
	5 Prostate	12.7	5 Rectum	13.9	5 Colon	22.2
All sites		204.3		235.0		265.3
Females						
	1 Breast	48.9	1 Breast	60.5	1 Breast	62.2
	2 Stomach	36.0	2 Cervix uteri	27.4	2 Cervix uteri	27.5
	3 Cervix uteri	29.0	3 Colon	24.3	3 Colon	27.3
	4 Colon	17.8	4 Skin	22.9	4 Skin	26.8
	5 Skin	13.5	5 Corpus uteri	16.9	5 Corpus uteri	16.9
All sites		252.1		266.7		275.0

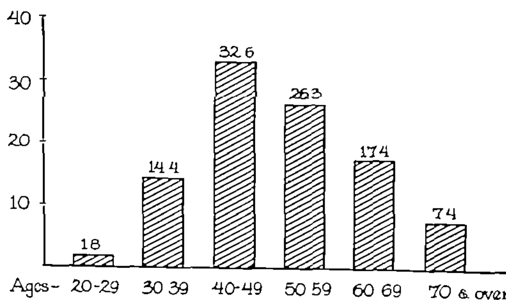


Chart 16 The age distribution in 1,544 patients with carcinoma of the breast in Presbyterian Hospital 1915–1942.

Morbidity data, however, are a much more accurate indication of the true frequency of breast carcinoma The two best sources of morbidity data are the cancer survey conducted under Levin's and Gerhardt's direction for the State of New York, and the Danish Cancer Registry under Clemmesen's direction Crude incidence rates for the five most frequently diagnosed cancers in each sex are shown in Table 33 for Denmark and for New York State, exclusive of New York City In both countries there is a higher incidence rate for breast carcinoma than for any other type of cancer in either sex Indeed, in the New York State figures the incidence of carcinoma of the breast among women is nearly twice the rate for malignancies of any other type or site in either sex From these data it would appear that about five percent of women in our society develop breast carcinoma at some time during their lives

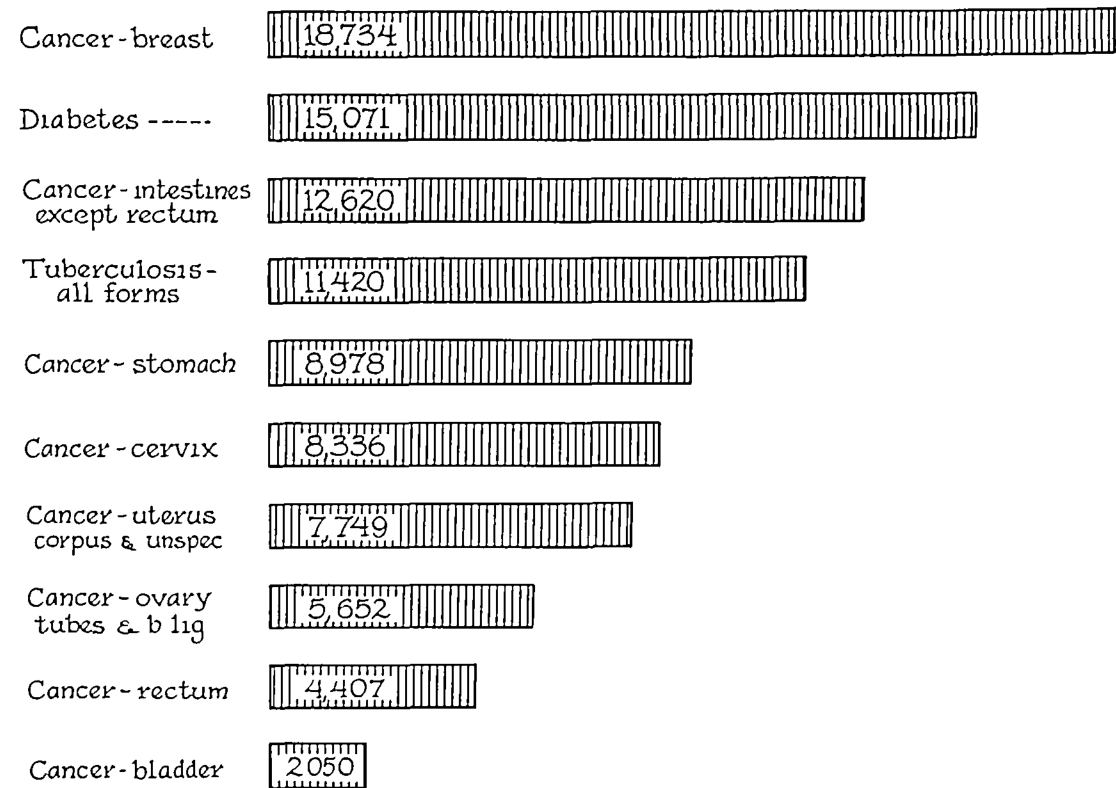


Chart 15 Mortality from breast carcinoma compared with that from other diseases

Age Distribution

The most accurate data regarding the age distribution of mammary carcinoma are to be obtained from morbidity data which record the age at which the disease was diagnosed, rather than from mortality data which record the date at which it terminates fatally The mortality data have two defects For one thing they take no account of cured patients, more of whom are found in the older age groups Secondly, our modern methods of palliation, particularly radiotherapy and hormone treatment, probably prolong life for some types of mammary carcinoma even when cure is not achieved, and the age at which death occurs is some years later than the date of onset

The age distribution of our Presbyterian Hospital patients with breast carcinoma during the years 1915–42 is shown in Chart 16

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	5 Prostate	12.7	5 Rectum	13.9	5 Colon	22.2
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	5 Skin	13.5	5 Corpus uteri	16.9	5 Corpus uteri	16.9
	All sites	252.1		266.7		275.0

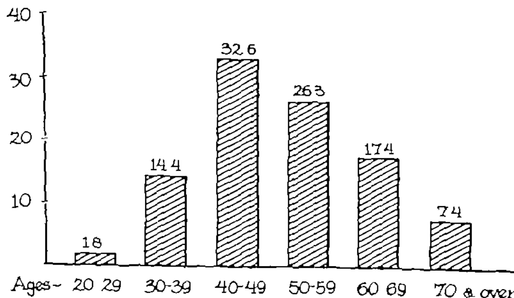


Chart 16 The age distribution in 1 544 patients with carcinoma of the breast in Presbyterian Hospital 1915–1942.

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then levels off for a five-year period, corresponding apparently to the menopause Then it climbs to reach a second peak after the age of 65, levels off again, and finally climbs sharply toward the end of the life span The New York State data show only a minor leveling off at the age of menopause

Jacobsen made a special study of the two-peaked feature of the age-incidence curve, and believed that he found an explanation In his data the patients who had a family history of mammary carcinoma constituted the group of cases forming the first peak at ages 45 to 50 The second peak at 65 was formed by patients who did not have family histories of cancer This suggests that a familial predisposition to the disease results in its developing at an earlier age

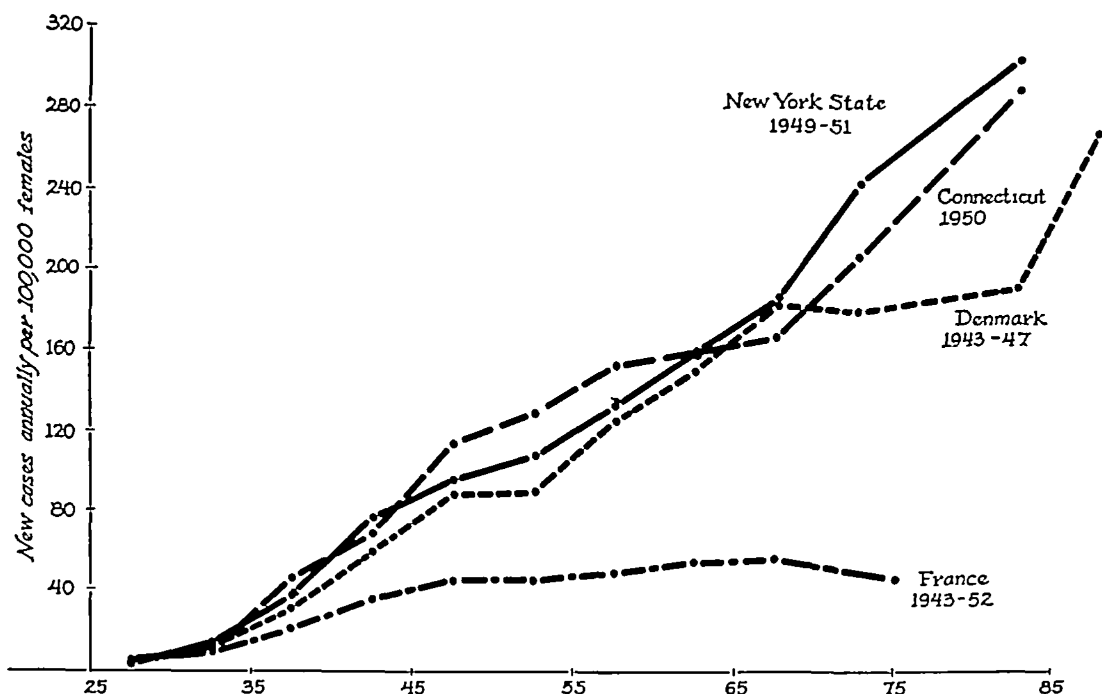


Chart 17 The morbidity of breast carcinoma by age

Morse studied this question not only in our Presbyterian Hospital data but also in Jacobsen's, and found that mammary carcinoma seems to develop approximately ten years earlier in the daughters of mothers who have had the disease than it developed in their mothers Since the publication of Morse's paper several other instances have come to our attention and we now have a list of 18 primary cases in which either daughter, mother, or both, came to the Presbyterian Hospital with information concerning the other's age at onset of disease These are listed in Table 34

The history of one of my patients illustrates this tendency

Mrs H G , a housewife aged 29, was admitted to the Presbyterian Hospital on the 22nd of March, 1940 She had a 2 cm tumor of the lower outer sector of the right breast, clinically typical of carcinoma Her mother had developed breast carcinoma at the age of 48 Her only sister had been operated upon for the disease when she was 28 Although our patient had been married for eight years she had never become pregnant Biopsy showed her tumor to be a carcinoma and radical mastectomy was done There were no axillary metastases

Seven months later at follow-up examination I found a 2 cm tumor of the upper outer sector of the left breast, clinically suggestive of carcinoma Biopsy showed this

tumor also to be carcinoma Left radical mastectomy was done on the 23rd of October 1940 Again there were no axillary metastases.

Seven years later she became pregnant and was delivered of a boy Now 15 years after her second radical mastectomy she remains well

Table 34. Mothers and Daughters with Breast Cancer
(Primary Cases, Presbyterian Hospital)

Hospital number	Mother's age	Daughter's age	Difference
30689	62	58	− 4
67803	37	23	−14
303789	68	42	−26
369458	40	39	−1
425318	75	55	−20
491458	61	50	−11
503041	50	60	+10
512971	66	68	+2
538632	41	36	−5
240498	65	34	−31
571316	37	37	0
574828	74	47	−27
382523	54	62	+8
605233	48	29	−19
651524	54	44	−10
309621	76	42	−34
791091	71	66	−5
703297	61	46	−15
727392	55	45	−10
666138	73	63	−10
999427	70	62	−8
870487	49	32	−17
042646	51	46	−5
066623	55	41	−14
888643	45	53	+8
128341	61	47	−14
136810	50	37	−13
171261	50	30	−20
			Av −10 9

VandenBerg has reported a similar case in which the mother developed carcinoma in one breast at the age of 45 and in the other nine years later She had two daughters both of whom developed bilateral breast cancer In one daughter the disease first appeared at the age of 26 and in the other daughter at the age of 39 The first daughter had a daughter who also at the age of 36 developed breast carcinoma

In the remarkable breast cancer family described by Wood and Darling the disease was bilateral and appeared at an average age of 32 years during four generations In the fourth generation it appeared in one woman at the age of 18 years.

In our Presbyterian Hospital material patients with a family history of breast cancer seem on the average to be younger than the general run of patients, although the difference is not so striking as in Jacobsen's series where family histories were more carefully assembled Among my own personal cases 17 per

cent of those whose mothers, aunts or grandmothers had had breast cancer were under forty years of age, as against 12 5 per cent in the entire group, 57 4 per cent were under fifty, as against 46 3 per cent in the whole group, and none was over seventy

Histories involving breast cancer in several generations are still too few to permit study of the age incidence in the third and fourth generations Obviously, however, this must be done before we have a clear picture of the effect of family history upon age trends

Carcinoma of the Breast in Youth

The incidence of carcinoma of the breast decreases sharply below the age of 30 In our P H data only 1 8% of our 1,544 patients were under the age of 30

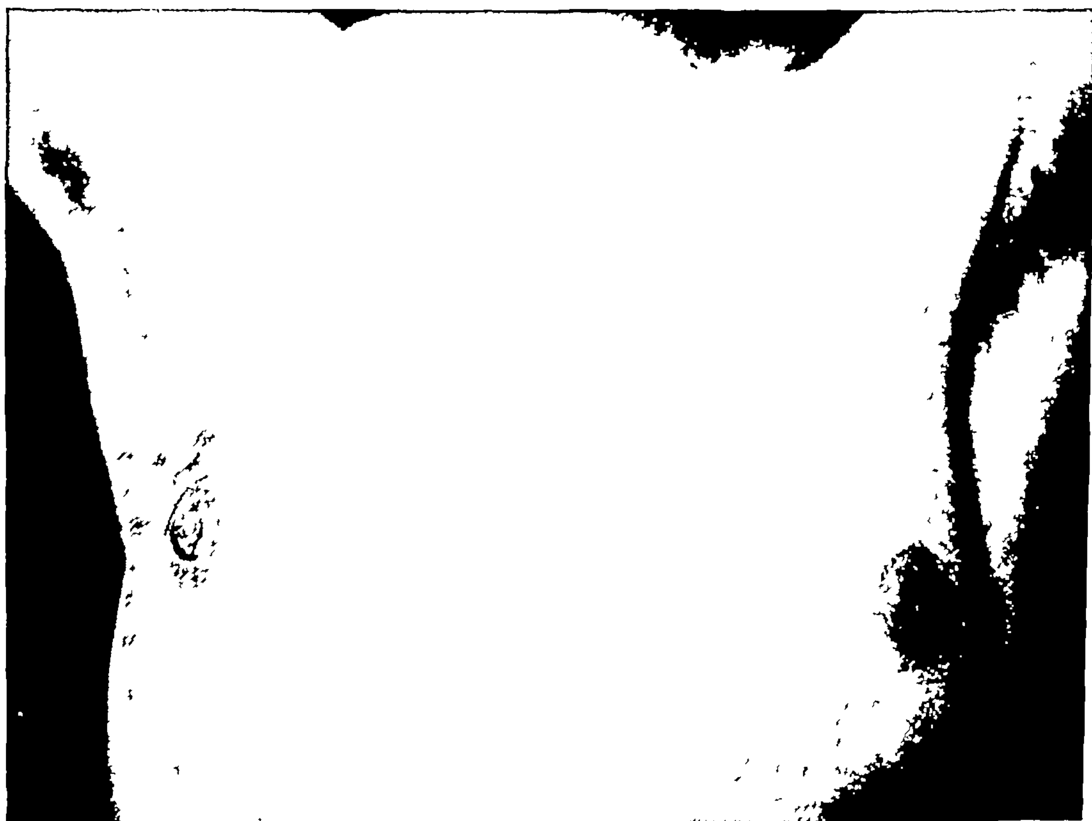


Fig 215 Carcinoma of the right breast in a patient aged 22

Below the age of 25 the disease is rare We had only four patients younger than 25 Our youngest patient was 22 years of age She had been aware of a small tumor in the outer portion of her right breast since early girlhood Three years previous to her admission to Presbyterian Hospital, when she was 20, she had become pregnant for the first time and the tumor had begun to enlarge It had grown steadily larger during her pregnancy and during the six months that she nursed her baby On admission the carcinoma of the upper outer portion of her right breast (Fig 215) was advanced It measured 4 x 5 cm in diameter and was fixed to the underlying chest wall The nipple was retracted and there was some redness of the overlying skin The axillary nodes were obviously involved Radical mastectomy was done Bone and liver metastases were apparent within four months, and the patient died six months after operation

Below the age of 20 carcinoma of the breast is a medical curiosity In Pirquet s monumental tabulation of English mortality data that included 70 257 deaths from breast carcinoma there was one case of a child under the age of 5 years, one case between the ages of 10 and 14 five cases between the ages of 15 and 19 and 27 cases between the ages of 20 and 24 Dr Stout has two hitherto unreported examples of carcinoma of the breast occurring in children in the records of the Laboratory of Surgical Pathology of the College of Physicians and Surgeons One of these children was three years old and the other 15 years old Both lesions were microscopically unquestioned carcinomas. Several remarkable features of the second case justify summarizing it here.



Fig 216. The microscopical appearance of carcinoma of the breast in a girl aged 15

A J S first came under the observation of Dr George H Semken when she was 9 years and 7 months of age She had had a tumor of the right breast since the age of 5 years. It was situated beneath the edge of the areola and extended lateral to it between the radii of 8.30 and 11 o clock.

Dr Semken observed the tumor for some six years, until the patient was 15 years and 10 months old, and the tumor had grown to about 3 cm in diameter The right breast, in which the tumor was situated was retarded in development.

On 4/12/45 he excised the tumor locally Dr Stout described it as a firm, sharply circumscribed nodule enclosed in a little fat It measured 25 x 18 x 13 mm. Microscopically it was a carcinoma composed of strands and cords of epithelial tumor cells that showed very little tendency to form acini but that anastomosed one with another to infiltrate the surrounding fat (Fig. 216) Mitoses averaged one in every five or six high power fields.

Eleven years later the patient was reported as being well. There had been no recurrence of the breast tumor despite the fact that only a very limited local excision had been done

A careful study of the reported cases of breast carcinoma below the age of 20 reveals that there are only a half dozen that have been described in sufficient detail to warrant their acceptance as genuine These are the cases of Thompson, Levings, Krauss and Klein, Carnett, Widmann and Howell, Nunn, and Sears and Schlesinger A highly malignant tumor occurring in a 15 year old girl, described by Chauvel and Renaud, was probably a malignant hemangio-endothelioma rather than a carcinoma Harrington, in his 1940 report on the results of 5,026 mastectomies for breast carcinoma, referred to five patients between the ages of 16 and 19 years, but gave no details regarding them Cholnoky collected data regarding breast cancer in youth from six large New York and Boston hospitals and found three patients, 12, 15 and 18 years old, respectively, with the disease He gave no details regarding them

It would appear that Semken's patient is unique in that her carcinoma was of ten years' known duration and was cured by nothing more than local excision This suggests that carcinoma developing in the breast before puberty may sometimes, like melanoma occurring before puberty, be clinically benign although histologically malignant

Breast Cancer in Old Age

Since the incidence of mammary carcinoma steadily rises with advancing age it is one of the most frequent diseases of aged women This feature of old age has recently been discussed by River, by David, and by Case

From the clinical point of view these facts suggest two rules First, any breast tumor appearing after the menopause is very likely to be carcinoma, since the incidence of benign lesions such as cystic disease decreases sharply after this point Second, the older the patient the greater her chances of developing breast cancer

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A careful study of the reported cases of breast carcinoma below the age of 20 reveals that there are only a half dozen that have been described in sufficient detail to warrant their acceptance as genuine These are the cases of Thompson, Levings, Krauss and Klein, Carnett, Widmann and Howell, Nunn, and Sears and Schlesinger A highly malignant tumor occurring in a 15 year old girl, described by Chauvel and Renaud, was probably a malignant hemangio-endothelioma rather than a carcinoma Harrington, in his 1940 report on the results of 5,026 mastectomies for breast carcinoma, referred to five patients between the ages of 16 and 19 years, but gave no details regarding them Cholnoky collected data regarding breast cancer in youth from six large New York and Boston hospitals and found three patients, 12, 15 and 18 years old, respectively, with the disease He gave no details regarding them

It would appear that Semken's patient is unique in that her carcinoma was of ten years' known duration and was cured by nothing more than local excision This suggests that carcinoma developing in the breast before puberty may sometimes, like melanoma occurring before puberty, be clinically benign although histologically malignant

Breast Cancer in Old Age

Since the incidence of mammary carcinoma steadily rises with advancing age it is one of the most frequent diseases of aged women This feature of old age has recently been discussed by River, by David, and by Case

From the clinical point of view these facts suggest two rules First, any breast tumor appearing after the menopause is very likely to be carcinoma, since the incidence of benign lesions such as cystic disease decreases sharply after this point Second, the older the patient the greater her chances of developing breast cancer

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Study of these data as to the size of the primary carcinoma in two periods, some fourteen years apart suggests that with the passage of time the diagnosis has been made when the primary tumor was smaller The measurements made by the pathologist are presumably more accurate, and the data show that during the 1915 to 1934 period less than one third of the patients had tumors measuring under 30 mm in diameter while during the 1935 to 1942 period approximately one-half had tumors of this size. The mean diameter of the tumors in both the clinical and pathological measurements, is somewhat smaller in the 1935 to 1942 period These facts give some hope that the detection and diagnosis of breast carcinoma is improving as time goes by

The primary focus is sometimes discovered while it is very small I have pointed out in discussing diagnosis that it is possible to detect a breast carcinoma by palpation when it is as small as 5 mm in diameter provided that it is not hidden in the depths of a large breast. Carcinomas smaller than this are found not by the clinician but by the pathologist in the course of his studies of tissue removed from the breast, usually for cystic disease or some other benign lesion The following case is an example

Mrs. E. M a widowed school teacher aged 44 was admitted to the Presbyterian Hospital for a tumor of the right breast of six weeks duration. I had operated upon her mother at the age of 70 for a carcinoma of the breast.

Her tumor was a firm but movable 4 x 3 cm. mass just beyond the areolar edge in the radius of 8 o clock of the right breast There was questionable slight skin dimpling over it. At operation the tumor was found to be a group of blue-domed cysts, the largest 1 cm in diameter lying in rather dense mammary tissue. The cysts and the adjacent breast tissue were excised A frozen section revealed nothing suspicious. The wound was therefore closed.

Nothing suggestive of carcinoma was noted in the gross study of the specimen but a number of blocks of tissue were cut for paraffin sections. The sections showed cystic disease and fibrosis One section only revealed a minute area of undoubted carcinoma. It is shown in low power magnification in Figure 217 Its total diameter was approximately 5 mm.

With this diagnosis a radical mastectomy was carried out. No residual carcinoma was found in the amputated breast, and there were no axillary metastases.

This case illustrates the value of the pathologist s studying the tissue removed from the breast with meticulous care, and of always making a number of microscopical sections. In Dr Stout s laboratory where this kind of study of surgical specimens has been the rule, one or two such minute breast carcinomas are discovered every year

Site Within the Breast

The reports of large case series of breast carcinoma which include data as to the site of the carcinoma show that the upper outer sector is much the most frequent site and the lower inner sector the least frequent. Some of these data, *including* our own Presbyterian Hospital data for the years 1915–1942, are summarized in Table 36

All these data as to the site of carcinoma in the breast, including our own from the Presbyterian Hospital are probably not very accurate because as I have explained in Chapter 5 they are based upon written descriptions rather than upon

CHAPTER 19

THE NATURAL HISTORY OF BREAST CARCINOMA

The Primary Focus

Breast carcinoma ordinarily originates as a single focus in one breast It is, however, true that we occasionally find two or more apparently separate foci of carcinoma when we section the operative specimens in the laboratory Dr Stout estimates the frequency of this finding as 5 per cent

The Size of the Primary Tumor

Unfortunately the primary focus of carcinoma in the breast is usually not diagnosed until it is several centimeters in diameter, and has presumably been present for many months Our data from the Presbyterian Hospital as to the size of the primary tumor on admission to the hospital are presented in Table 35 They are divided into two groups, the data for the period 1915 to 1934, and those for 1935 to 1942 The clinical measurements, as well as the measurements made by the pathologist studying the surgical specimen, are shown

Table 35 Size of Primary Carcinoma in the Breast
(Presbyterian Hospital)

Size	1915–1934				1935–1942			
	Clinical meas		Patholog meas		Clinical meas		Patholog meas	
	Number of cases	Per cent cumulated	Number of cases	Per cent cumulated	Number of cases	Per cent cumulated	Number of cases	Per cent cumulated
Under 11 mm	17	2 2	28	5 4	6	1 0	14	3 2
11–19 mm	14	3 9	37	12 5	13	3 0	67	18 5
20–29 mm	73	13 2	101	31 9	71	14 4	135	49 3
30–39 mm	123	28 7	106	52 3	110	32 0	96	71 2
40–49 mm	104	41 9	69	65 6	117	50 7	53	83 3
50–59 mm	110	55 8	75	80 0	81	63 7	23	88 6
60–69 mm	143	73 9	36	86 9	69	74 7	24	94 1
70 mm and over	206	100 0	68	100 0	158	100 0	26	100 0
Total number cases	790		520		625		438	
Mean diameter	5 4 cm		4 1 cm		4 8 cm		3 4 cm	

mastectomy between the years 1935 and 1950 In these cases I sketched the breast and the position of the tumor within it and I am therefore able to locate the tumor precisely Figure 218 shows the percentage of these carcinomas in the seven different breast zones described in Chapter 5 which seems significant in the light of our present day knowledge of the routes of spread of breast car cinoma. It is of interest that the number of carcinomas occurring in the upper and lower parasternal zones as I have defined them is very small indeed and that the number of central tumors is comparatively large

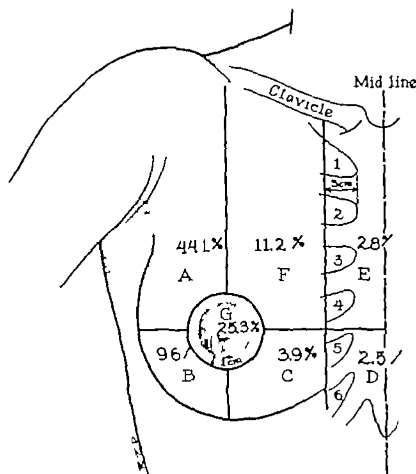


Fig 218 The distribution of carcinoma in the seven different breast zones (personal series of cases)

The upper outer sector of the breast is in my own data as in those from other sources, the site of almost one-half of all the carcinomas It may be argued that this sector contains a greater bulk of breast tissue than any of the other three quadrants that is, the greatest number of cubic centimeters of mammary gland exposed to the risk of carcinomatous change This is a purely anatomical explana tion but I know of no other

The Side Affected

The fact that carcinoma develops more often in the left than in the right breast was emphasized by Lane Claypon (1926) in her comprehensive studies of etiological factors Busk and Clemmesen have investigated the question utilizing 4 139 cases of breast carcinoma in females recorded in the Danish Cancer

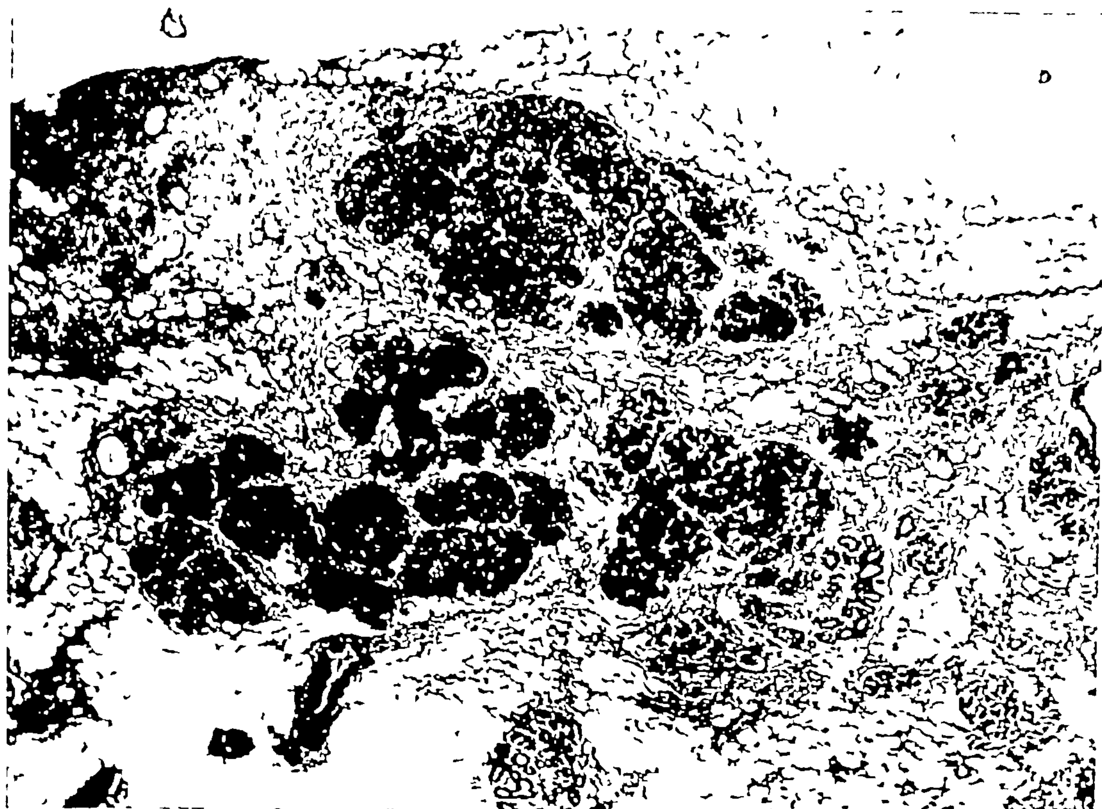


Fig 217 A minute breast carcinoma discovered at microscopic examination of breast tissue removed for cystic disease

Table 36. Site of Carcinoma within the Breast

Case series	Number of cases	Upper outer	Lower outer	Upper inner	Lower inner	Central	Diffuse	Axillary tail
Lane-Claypon (1928)	1,354	30 6%	8 9%	12 3%	4 3%	14 3%	4 7%	
Truscott (1947)	836	46 %	12 %	20 %	5 %	13 %		4%
Harnett (1948)	2,129	43 %	9 6%	13 3%	4 4%	11 %	15 2%	
Nohrman (1949)	591	47%		18%		35 %		
Smithers (1952)	662	47 7%	8 8%	14 8%	6 %	22 8%		
Presbyterian Hospital (1915–1942)	1,421	47 4%	10 6%	16 2%	6 2%	13 8%	5 8%	

actual sketches of the breast Moreover, the frequency of parasternal and central carcinomas, based upon precise definitions of these anatomical zones, cannot be determined at all from these data

In our effort to arrive at a more exact estimate of the site of carcinoma in the breast I have turned to the records of my 356 personal cases treated by radical

mastectomy between the years 1935 and 1950 In these cases I sketched the breast and the position of the tumor within it and I am therefore able to locate the tumor precisely Figure 218 shows the percentage of these carcinomas in the seven different breast zones described in Chapter 5 which seems significant in the light of our present day knowledge of the routes of spread of breast car cinoma It is of interest that the number of carcinomas occurring in the upper and lower parasternal zones as I have defined them is very small indeed and that the number of central tumors is comparatively large

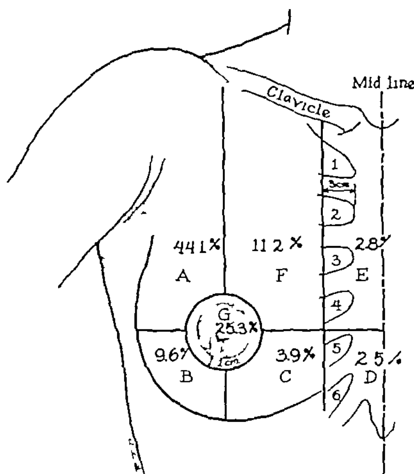


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Registry between the years 1942 to 1946, 1,045 cases from the Swiss Cancer Census for 1933–35, and 5,618 deaths from breast cancer recorded by the Registrar-General for England and Wales during 1931 to 1934 They concluded that carcinoma of the left breast is 11 per cent more frequent than carcinoma of the right breast

Our own Presbyterian Hospital data confirm the predominance of left-sided breast carcinoma Of our 1,523 breast carcinomas (1915–1942) 796 developed in the left and 727 in the right breast This gives a ratio of 109 49 to 100 in favor of the left side

The reason for the greater frequency of carcinoma in the left breast remains an enigma Lane-Claypon suggested that the protection from trauma that the right arm provides for the right breast is a factor I doubt this explanation

Bilateral Origin

Both breasts may be involved by carcinoma under two different circumstances First of all, the disease may originate in one breast and extend to the opposite one, either by permeation of lymphatics across the midline, or by generalized metastasis through the blood stream This is a frequent event in advanced and terminal breast carcinoma and is not a phenomenon requiring any special discussion

A second type of involvement of both breasts is this development of independent primary carcinoma in both breasts The two lesions may develop simultaneously or successively Simultaneous involvement is rare Successive involvement of the second breast has an appreciable frequency which warrants close study

The question of whether the carcinoma in the second breast is indeed primary, and not an extension or recurrence of the primary tumor in the other breast, rests upon both histological and clinical evidence If the carcinomas in each breast are clearly different histological types, it may be presumed that they are of independent origin This is an infrequent finding, however Most breast carcinomas are so much alike that it is impossible to be certain that any two are of different origin The clinical fact that there is no evidence of local recurrence or regional or distant metastasis of the primary carcinoma in the one breast provides the strongest argument that the carcinoma in the other breast is a new and independent primary tumor Cases of doubtful nature should be regarded as metastatic

McWilliams collected a total of 98 bilateral breast carcinomas, defined in these terms, from some 40 different surgeons The fact that 32 per cent of the patients with successive bilateral carcinoma whose histories McWilliams collected developed the disease in the second breast within a year after it had appeared in the first breast, suggests to me that some of these were not new and independent carcinomas but merely extensions of the original carcinoma Moreover, McWilliams' figure of 4 7 per cent of successive bilateral carcinoma is rather high in comparison with other recent careful studies of the frequency of bilateral carcinoma based upon data from individual clinics, summarized in Table 37

Table 37 Bilateral Primary Breast Carcinoma

Author	Year	Total Number of patients breast carcinoma	Simultaneous bilateral No	Simultaneous bilateral Per cent	Successive bilateral No	Successive bilateral Per cent
Kilgore	1921	1 100			13	1 1
Greenough	1921	639	5	0 7	11	1 6
McWilliams	1925		11	0 2	87	4 7
Bérard	1939	645	10	1 5	11	1 6
Harrington	1946	6,559	62	1	212	3 4
Desalve	1949	1,259	9	0 7	46	3 6
Smithers	1952	1 777	11	0 6	42	2 4
Reese	1953	504			15	3
Guiss	1954	1,521	2	0 1	19	1

Our Presbyterian Hospital data regarding bilateral breast carcinoma are shown in Table 38

Table 38. Bilateral Primary Breast Carcinoma

(Presbyterian Hospital 1915–42)

1,544 Patients with breast carcinoma

Bilateral and simultaneous	6 cases, or 0 4%
Bilateral and successive	29 cases, or 1.9%
Total bilateral	35 cases, or 2.3%

These data indicate that approximately 3 per cent of women who develop carcinoma in one breast also develop it simultaneously or later on in the second breast. Their chance of developing the disease in the second breast is somewhat greater than that of women in the general population, but it is probably not greater than women with a familial history of breast carcinoma have of developing carcinoma in one breast

A generation ago Kilgore and more recently Pack have advocated prophylactic removal of the second breast to safeguard the patient against carcinoma developing in it. Pack has suggested that this would improve the cure rate of breast cancer by 7 5 per cent. His argument is not supported by the facts Primary carcinoma develops in the second breast in some 3 per cent of patients and only about half of these could be safeguarded from this hazard by its prophylactic removal The other half are unfortunately doomed to succumb to the carcinoma in the breast first involved Even when carcinoma does develop in the second breast the patient has a good chance of cure if it is found at an early stage by careful follow up Women much prefer not to lose their one remaining breast, and I do not believe we have sufficient evidence to advise them to do so

Although carcinoma in the second breast is not frequent enough to justify its prophylactic removal it is frequent enough to necessitate careful and lifelong follow up examination of the second breast If the patient is not capable of examining her second breast herself every few months it should be examined at least every six months by a physician

The interval between the development of carcinoma in the first breast and in the second breast is often long In our series of cases the average interval was

8 years The shortest interval was 1 7 years and the longest 32 5 years The story of one of these patients with a long interval is an interesting one

Mrs M L, a housewife aged 40, was admitted to Presbyterian Hospital with a 1 cm carcinoma of the lower inner sector of the right breast Radical mastectomy was done

She had no further evidence of breast disease for thirty-one years, until examination in the follow-up clinic revealed a small area of skin retraction in the upper outer sector of the left breast There was a small area of induration beneath the retraction At this time she was 70 years of age The new lesion in the left breast proved to be a carcinoma, and radical mastectomy was done No metastases were found in 15 axillary lymph nodes Two years later she continued well



Fig 219 The stellate configuration of a small carcinoma of the breast

The Spread of the Disease in the Breast

The primary focus of carcinoma within the breast grows by division of its constituent cells which infiltrate the tissues of the breast The infiltration tends to be along ducts, along fascial strands, and into the less resistant mammary fat The carcinoma thus tends to have an irregular or stellate, rather than a round, outline, as in Figure 219 which shows an entire carcinoma in low magnification There are of course certain types of carcinomas, which I will describe separately, that are exceptions to the rule As the carcinoma cells multiply, they appear to stimulate proliferation of fibroblasts from the breast stroma, so that in

the majority of breast carcinomas the carcinoma cells lie in a dense fibrous matrix (Fig 220) This fibrous matrix is what gives breast carcinomas their dense consistence MacCarty believed that he could correlate the degree of fibrosis in and about breast carcinomas with their degree of malignancy but we have not been able to confirm his theory I will discuss this question of microscopical grading in Chapter 25

Extension of the disease within the mammary ducts is often seen I am not now referring to the special type of intraductal carcinoma in the collecting ducts of the nipple that characterizes the Paget s type of carcinoma I refer to the extension of breast carcinoma within ducts in the region of the primary tumor and

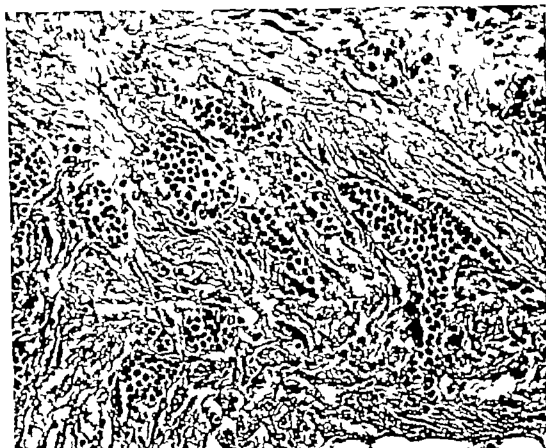


Fig. 220 Mammary carcinoma growing in a dense fibrous matrix.

sometimes far into the other parts of the breast Figure 221 shows carcinoma growing along a duct that has been cut longitudinally

One of the striking microscopic features of breast carcinoma is malignant transformation of the epithelium of an entire lobule, the lobular architecture still being preserved. Figure 222 shows this kind of cancerization of a lobule. If carcinoma reaches the epithelium of the terminal acini by growing along the duct lumens the process of intraductal spread must be a very extensive one, indeed There is, of course, another possible explanation for the phenomenon namely that carcinomatous transformation develops as a generalized phenomenon throughout ducts and acini in a wide segment of the breast. This must be the way in which carcinomas that are primarily intraductal originate In these neoplasms such a wide area of duct epithelium is involved that it is unreasonable

Fig 221 Mammary carcinoma growing along a duct



Fig 222 Mammary carcinoma involving an entire lobule

to assume that the disease originated from a mutation in a single cell at one point in the epithelium of any one duct

Carcinoma extending locally in the breast regularly infiltrates the mammary fat Figure 223 shows this phenomenon It would appear that fat offers very little resistance to the disease

Fraser who carried out interesting studies of the spread of the disease in the breast by means of whole sections and key block sections, emphasized the frequency of infiltration along fascial planes He pointed out that one side of a fascial line is often infiltrated while the other side is free indicating that the cancer cells follow the lines of least resistance Fraser emphasized the comparative immunity of muscle against invasion by carcinoma cells In advanced cases where

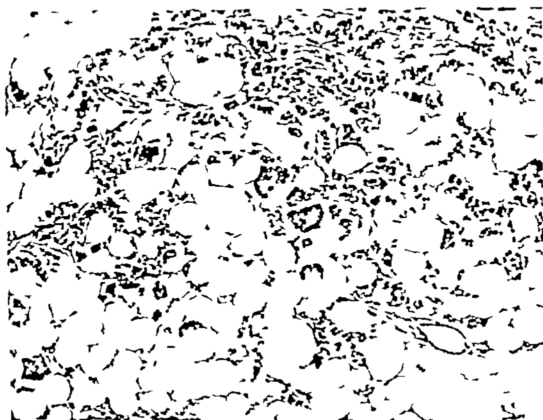


Fig 223 Mammary carcinoma infiltrating in fat.

the cancer rests upon the pectoral muscle and infiltrates the pectoral fascia extensively the muscle tissue itself is usually not involved

Extension of carcinoma within the breast also occurs through the lymphatics Thorough microscopical study of breasts removed for carcinoma will occasionally reveal the disease in indubitable lymphatics, as seen in Figure 224 but it is sometimes difficult to be certain whether the focus of carcinoma cells is lying in a tissue space or in a lymphatic. One of the easiest types of lymphatic invasion to recognize is that which occurs in perineural lymphatics, as illustrated in Figure 225 The periductal lymphatics also provide a route for lymphatic spread Figure 226 shows an embolus of carcinoma cells in a dilated periductal lymphatic

I have described the anatomy of the lymphatics of the breast in an earlier

Fig 224 Mammary carcinoma in a lymphatic

Fig. 225 Mammary carcinoma growing in perineural lymphatics

chapter The experiments in which dye has been injected into the breast have shown that it flows centripetally and localizes in the subareolar region

The microscopical studies of actual disease in the breast have, however, given a different impression of the route of lymphatic extension In his whole breast studies Fraser found that lymphatic invasion occurs first in a vertical direction down through the whole thickness of the breast to the retromammary fascial plane, from whence the distribution is in a centrifugal direction Fraser stated "In whatever portion of the breast the primary tumor may originate, this scheme of primary vertical distribution is apparent Figure 227 is a drawing



Fig. 226 A mammary carcinoma embolus in a periductal lymphatic.

made from Fraser s photograph which shows this vertical lymphatic dissemination of a breast carcinoma downward to the pectoral fascia, as seen in a whole breast section

Sampson Handley whose studies of the lymphatic spread of breast carcinoma were among the most extensive that have been made, also came to believe that the main direction of lymphatic spread in the breast is not centripetally to the subareolar plexus but vertically downward to the lymphatic plexus in the deep pectoral fascia underlying the breast.

In describing the further extension of carcinoma through the lymphatics of the breast, I can do no better than to quote further from Fraser

"Having gained entrance to the lymph stream, tumor cells evidently multiply with rapidity so that in a short space of time the main central lymphatics become filled and effectually plugged with them. Under these conditions the obstruction

which now exists to the normal lymph flow results in an opening up of a number of subsidiary channels which, though minute in size, have existed throughout the breast tissue, and particularly in the periductal and periacinar tissues Quantities of minute cancer cell groups enter these enlarging subsidiary channels, and so a widespread and general lymphatic distribution arises throughout the breast From what we have observed, the more general invasion is always secondary to

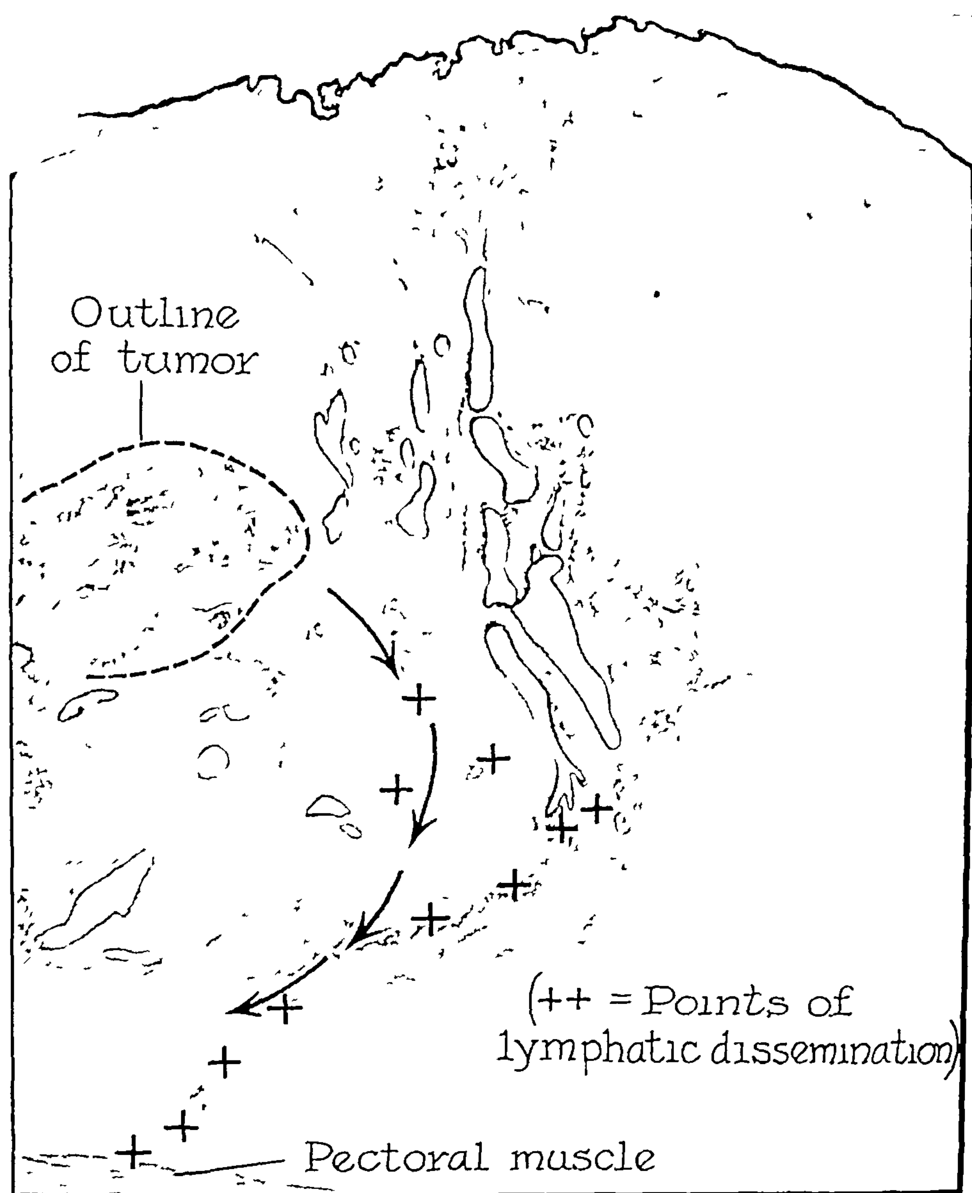


Fig 227 Lymphatic dissemination of breast carcinoma vertically downward to the pectoral fascia, as seen in a whole breast section (after Fraser)

the invasion of the central lymphatics (which penetrate vertically downwards through the center of the breast to the retromammary fascia) and their occlusion by growing cancer plugs "

Carcinoma also grows through the walls of blood vessels as it extends in the breast, and we sometimes see carcinoma emboli within the lumens of arteries as well as veins Figure 228 shows a large carcinoma embolus in the lumen of a good-sized sclerotic artery Figure 229 shows two small veins filled with carci-

Fig 228 Mammary carcinoma growing in a sclerotic artery



Fig. 229 Mammary carcinoma filling two small veins.

noma Delbet and Herrenschmidt wrote a good description of a breast carcinoma that showed a special tendency to grow within blood vessels

The Rate of Growth of Breast Carcinoma

We have very little knowledge of the rate of growth of breast carcinoma as indicated by actual measurements of the increase in size of the untreated primary tumor It might be supposed that each breast carcinoma has a growth rate that is more or less constant from the date of its origin as a mutation from a single cell We know that some breast carcinomas grow slowly and others rapidly but just what these growth rates are we do not know Richards estimates that the *average* mammary carcinoma increases 1 cm in size every three months He has correlated actual measurements of tumor size with the patients' statements as to tumor duration in a series of 324 breast carcinomas and has drawn up Table 39 which suggests that slowly growing tumors are much more curable than rapidly growing ones

Table 39. Rate of Growth vs. Survival in Mammary Carcinoma, 1939-1941

(Richards, 1948)

Rate of growth	Total number of cases	Alive after 5 years
SLOW Less than 1 cm per 6 months	55	84%
MODERATE 1 cm per 6 months	104	63 5%
FAST More than 1 cm per 3 months	139	18%
RAPID (Inflammatory)	26	4%
Total	324	43%

Collins has made some very shrewd and interesting speculations regarding the rate of tumor growth He has observed that the time it takes for a pulmonary metastasis to double in size varies with different types of tumors For breast carcinoma the doubling time was twenty-eight days Based on calculations of cell size, 30 doublings are required for a tumor originating from a single cell to reach a diameter of 1 cm From these facts Collins assumes that most cancers have been present for a very long time before they become evident clinically If Collins' theory is correct, and it has much to support it, these facts present an added challenge to us in terms of early diagnosis They also provide an explanation for the long latent period in the development of recurrence and metastases observed in some cases

Infiltration and Ulceration of the Overlying Skin

In the course of its local infiltrative growth within the breast the carcinoma, finally, in many patients who come for treatment late, reaches the overlying skin Immobility of the skin over the tumor and localized redness are signs that the

infiltration of the skin has begun Ulceration follows after a varying period of time The typical ulcer has raised, reddish edges and a crusted or necrotic, depressed base (Fig 230) In the majority of patients the ulcerated area enlarges very slowly and is not much of a surgical dressing problem In occasional patients however the ulcerative process progresses more rapidly and a large, foul smelling, fungating tumor results, which constitutes an exceedingly difficult therapeutic problem Hemorrhage sometimes severe is an occasional added complication Figure 231 shows a long neglected far advanced massive breast carcinoma, solidly fixed to the chest wall that bled profusely

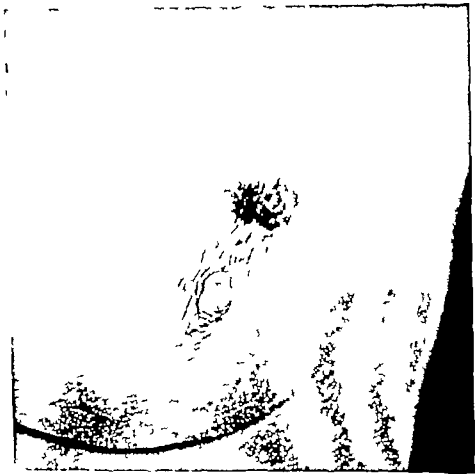


Fig 230 Small ulcer over carcinoma of the breast.

Satellite Nodules in the Skin over the Breast One of the indications of comparatively extensive carcinomatous involvement of the breast itself is the appearance of satellite nodules of carcinoma in the skin of the breast. Figure 232 shows such nodules around a carcinoma of the lower portion of the breast. They are not a part of the phenomenon of widespread and distant metastasis to the skin seen in the terminal stage of breast carcinoma. They are a local manifestation of the disease in the breast, and result from extension of the disease along lymphatics or ducts or fascial strands which lead the carcinoma into contact with the skin at some little distance from the primary focus They indicate therefore, that the disease is widespread within the breast

Edema of the Skin. Edema of the skin over the breast is an important clinical

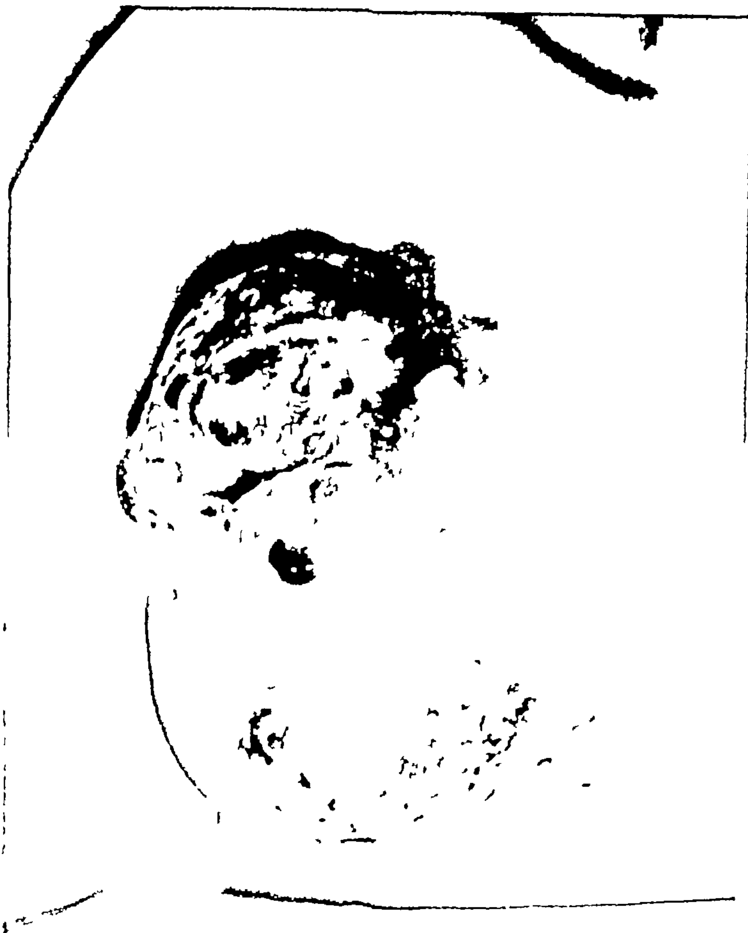


Fig 231 Massive fungating, bleeding carcinoma of the breast

Fig 232 Satellite skin nodules around an ulcerated carcinoma of the lower portion of the breast

phenomenon that develops in the course of breast carcinoma It has been called pigskin by the English and peau d orange by the French but *edema* is a more accurate name because it identifies the nature of the phenomenon There has been surprisingly little attention given to the pathology of edema of the skin and its significance in mammary carcinoma Leitch published a brief description of the microscopical findings many years ago but no one has written adequately about it. In Dr Stout s laboratory we have long been interested in the pathological mechanism by which edema of the skin is produced and we have made a special effort over a period of years to study microscopical sections of the edematous skin in these cases We have found that the skin is of course greatly thickened by edema in the corium At an early stage of the process the lymphatics of the deep



Fig 233 Carcinoma emboli in a dilated lymphatic in the corium of edematous skin The insert at the left shows in higher magnification the dilated lymphatic with its emboli from the lower central part of the section.

network in the corium are dilated and contain occasional emboli of carcinoma cells, as seen in Figure 233 At this early stage the edema involves only a limited area of the skin over the breast usually the lower half of the areola or the skin just caudad to it Gravity is no doubt a factor in the predisposition of this area of skin over the breast to edema.

At a later stage, when the skin edema is very extensive the smaller more superficial lymphatics as well as the deeper ones in the corium are filled by carcinoma cells as seen in Figure 234 We infer that the deep lymphatics of the corium are at first partially blocked by embolism and finally solidly occluded by permeation with carcinoma cells In edematous skin we have not seen carcinoma diffusely invading either the epidermis or corium The disease is confined within the lymphatics, and it produces edema of the skin by blocking them

Carcinoma "Telangiectaticum" or "Erysipelatodes"

An unusual form of involvement of the skin in far advanced breast carcinoma has been called carcinoma "telangiectaticum" or "erysipelatodes" Purplish-red, raised nodules appear in the skin over the breast or adjacent chest wall or neck, and fuse to form broad reddish indurated areas On microscopical study these nodules are seen to be dilated, thin-walled vessels situated very superficially in the epidermis and filled with carcinoma cells The first good descriptions of this disease picture were written by Kuttner, Rasch, Weber, Savatard, and Leavell and Tillotson More recent case reports by Pfahler and Case, Dawson and Shaw, and Camiel and Bolker have included detailed microscopic studies that attempt to determine whether the dilated tumor-containing vessels in the epidermis are



Fig 234 Mammary carcinoma in the superficial lymphatics of edematous skin

capillaries or lymphatics Dawson identified them as both blood and lymph vessels Camiel and Bolker concluded that they are lymphatics

This *telangiectatic* or *erysipelatoid* lesion should not be confused with the inflammatory type of breast carcinoma, as Chris has recently done The former is a skin manifestation in far advanced late mammary carcinoma, usually recurrent after mastectomy or irradiation The latter is a primary clinical form of breast carcinoma in which the breast, from an early stage in the evolution of the disease, is enlarged and indurated, and the skin over it is generally reddened and edematous I will deal with the inflammatory type of carcinoma in Chapter 24

Carcinoma "en Cuirasse"

Velpeau's attention was first attracted in 1838 (he states) to a special form of carcinomatous involvement of the skin to which he gave the striking name "en

cuirasse I cannot improve upon Velpeau s description It involves a single area, or sometimes several isolated small areas of subcutaneous tissue and skin The involved area feels hard rough, stiff and thickened It has an abnormal reddish color and a stippled appearance. The skin looks as if it had been tanned, or as if a portion of stiff leather had replaced the natural skin The small disseminated plaques have the same characteristics, and look like violet red spots.

Usually the larger plaques are surrounded by a multitude of these small ones. I have seen patients whose breasts were completely covered with the plaques and in whom the wooden-like change extended up to the hollow of the axilla on one side, towards the clavicle, and across the sternum to the other side. "

"At its onset this primary scirrhus of the skin does not attract the attention of patients because it causes no pain and there is no exudate. Since the skin alone is affected it is not noticed until it is fairly well advanced The physician, how ever should never be deceived and I cannot too strongly urge him to be on guard when he notices in the skin over the chest of women patients, a yellowish red marbling, or stippled gray patches scattered here and there, especially if they are permanent and instead of being supple and disappearing with pressure, they are hard, thick inelastic, or wooden like Despite their benign appearance these spots are cancer of the worst kind. Although at first separate they eventu ally fuse together forming plaques of larger and larger size and finally a true cuirasse

When modern students of breast cancer such as Sampson Handley began to investigate "en cuirasse microscopically they found that the epidermis is atrophied and the corium is greatly thickened by edema and fibrosis and by lymphocytic infiltration around blood vessels and lymphatics These changes, and the pigmentation which is such a striking feature of the lesion are similar to those that develop in the lower legs of patients with lymphatic obstruction due to circulatory difficulties At a later stage of "en cuirasse, when nodules and ulcers have developed in the involved skin actual carcinomatous infiltration of the thickened skin is of course found

The clinical characteristics of carcinoma en cuirasse are illustrated by the following case

L. F a 57 year old housewife, came to the Presbyterian Hospital in May 1919 with a large carcinoma of the left breast with massive axillary metastases. A radical mastec tomy was nevertheless done. Local recurrence appeared on the chest wall twenty months later and evolved in the "cuirasse" shown in Figure 235 The cuirasse, out lined with a skin pencil, has involved the entire operative field and extended medially across the sternum to most of the skin over the opposite breast, upward over the clav icle to the supraclavicular skin, and laterally around to the skin of the back. The patient died four years and eight months after operation

Fortunately the en cuirasse form of carcinoma is not often seen today The primary carcinoma can usually be controlled by either surgery or irradiation and does not get out of hand as it did in Velpeau s time

Carcinomatous Fibrosis of the Breast

The primary carcinoma in the breast does not always grow expansively and form a bulky and sometimes ulcerated tumor In occasional cases the fibrotic



Fig 235 Carcinoma "en cuirasse"

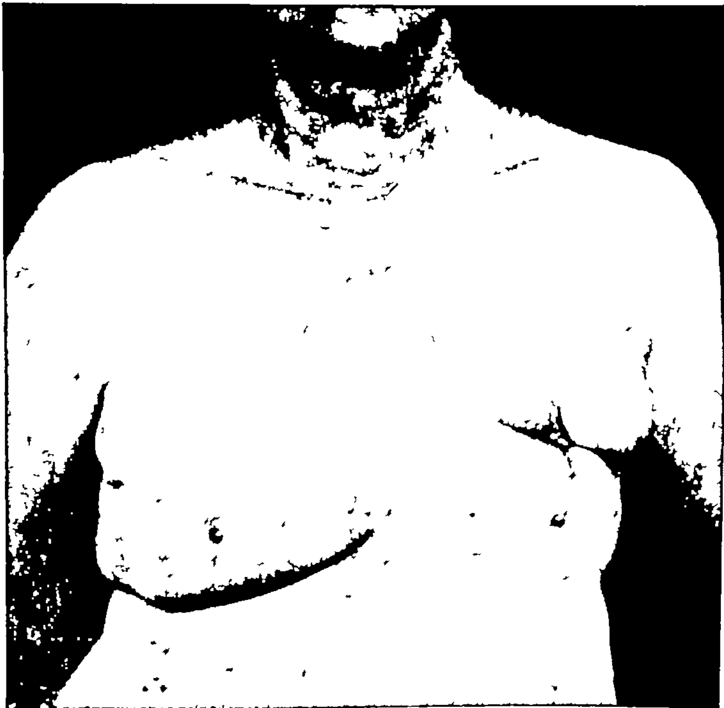


Fig 236 Breast contracted by carcinomatous fibrosis

reaction in the breast to the presence of the carcinoma is so marked that the breast shrinks rather than enlarges What was once a comparatively large, dependent, soft and movable breast becomes a hard, flattened, shrivelled organ, solidly fixed to the chest wall Figure 236 shows this kind of carcinomatous fibrosis of the breast occurring in Mrs R P, an 82 year old widow

She had first noted retraction of the left nipple twelve years previously During the following years the breast had slowly contracted She had not consulted any physician and had no treatment As the photograph shows her left breast was greatly shrunken It had not been destroyed by ulceration because there was none but by the slow process of replacement of the mammary fat and parenchyma The areola could no longer be identified The nipple was reduced to a papillary nubbin in the depths of a stellate depression Beneath this central depression there was a firm 5 cm tumor The shrunken breast and the tumor within it were movable over the chest wall A single, firm, movable 1 cm node was palpable in the axilla Since this patient s slow growing breast carcinoma gave her no symptoms it was not treated She died two years after I first saw her and fourteen years after the onset of her breast carcinoma of general debility

The Method of Extension of Mammary Carcinoma

Embolism or Permeation A description of the local extension and the regional lymph node metastasis of breast carcinoma must include a discussion of the method by which the disease extends along lymphatics Until Sampson Handley carried out his studies of this question at the Middlesex Hospital in the early years of the century it was generally assumed that carcinoma cells disseminate through lymphatics by embolism All pathologists have occasionally seen these emboli in lymphatics in or adjacent to the primary tumor as well as in the peripheral sinuses of lymph nodes The lymphatic trunks between the breast and the regional lymph nodes are usually found however to be free of carcinoma. It seems reasonable to conclude that the carcinoma emboli escape through them leaving no trace of their passage

Handley concluded however that permeation rather than embolism is the usual method of dissemination In his words Cancer spreads by permeating the lymphatic system like an invisible annular ringworm The growing edge extends like a ripple in a wider and wider circle within whose circumference healing processes take place so that the area of permeation at any one time is not a disc but a rim the advancing microscopic growing edge of the cancer owing to the failure at isolated points of the defensive process of perilymphatic fibrosis, may leave in its track here and there, isolated secondary foci which give rise to secondary macroscopic metastases

Handley documented his thesis with excellent descriptions and photomicrographs, and there can be no doubt but that in some patients, particularly those with advanced and terminal breast carcinoma, permeation of lymphatics is seen It was such cases in general that Handley studied

But the permeation theory has not withstood critical evaluation. Sampson Handley s contemporaries such as Fitzwilliams and Fraser equally devoted students of breast carcinoma did not accept it, and continued to believe that embolism is the usual method by which breast carcinoma disseminates at least in its earlier and operable stage Present day pathologists in general take this view It is certainly my own belief

The Epigastric Route to the Liver

A special type of local extension of breast carcinoma to the liver through the epigastric angle was described by Sampson Handley He pointed out that the lower inner border of the breast overlies the sixth costal cartilage, and that this



Fig 235 Carcinoma "en cuirasse."

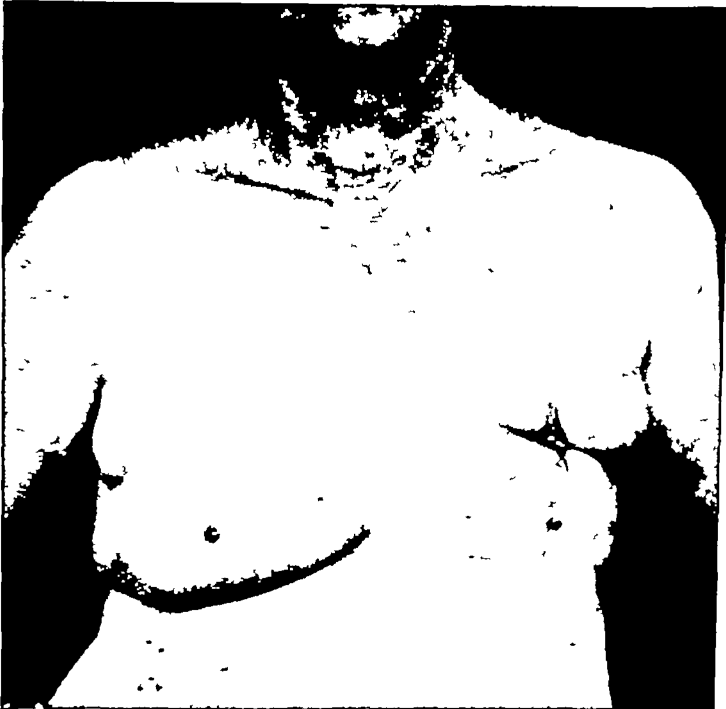


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and infiltrates the surrounding fat Since the extent and distribution of regional lymph node metastases is a question of critical importance in the choice of therapy for breast carcinoma I shall discuss it in detail

Although many lymph nodes containing metastases are enlarged and the disease in them is grossly obvious metastases are not infrequently found microscopically in very small lymph nodes measuring only a few millimeters in diameter

The customary method of determining the presence of metastases in a lymph node has been to study microscopically one section through its greatest diameter Because the volume of section cutting is so great that the technicians in laboratories are always pressed only one section is cut through each node, even though it is obvious that we may well miss a small focus of carcinoma in an uncut part of a node. Saphir proved the inadequacy of one level sectioning by an experiment in which he recut in serial section the lymph nodes in a series of 30 cases of breast carcinoma in which previous single level sections had not shown metastases An average of 332 sections were cut through each node. By serial section Saphir found metastases in 10 or 33 per cent of the cases

Pickren has repeated and expanded this experiment in Dr Stout s laboratory by recutting the nodes in 33 cases in which previous one-level sectioning had not shown metastases Pickren recut the nodes in several sections each 15 microns thick. An important point of difference between Saphir s and Pickren s studies is that Saphir had only an average of 5 nodes per case, while Pickren who used the clearing technique for finding nodes, had an average of 37 per case, or a total of 1211 nodes. Pickren found metastases in 6 or 18 per cent, of his cases These data are summarized in Table 40 They prove beyond doubt that our routine

Table 40 Results of Multiple Level Sections through Lymph Nodes in Which Single Level Sections Were Negative

Author and clinic	Number of cases studied	Number of nodes per case	Total number of nodes studied	Cases with positive nodes—single level	Cases with positive nodes—multiple levels
Saphir O., Chicago	30	5	149	0%	33%
Pickren, Presbyterian Hospital, N Y	33	37	1211	0%	18%

method of studying lymph nodes has missed metastases in a considerable proportion of cases. This is one explanation for the occasional appearance of distant metastases in patients in whom no axillary metastases were found

Axillary Lymph Node Metastasis

The main route for lymphatic metastasis from breast carcinoma is through the axilla. In most patients the axillary nodes are the first to be involved in the regional spread of the disease, and for a period of time they are the only regional nodes involved. The best proof of this is the fact that a considerable proportion

point is only about an inch from the ensiform cartilage, where subperitoneal fat lies immediately beneath the fascia of the linea alba In several cases which he illustrated with excellent drawings and photomicrographs, Handley traced breast carcinoma permeating lymphatics in the rectus sheath and muscle to reach the region of the tip of the ensiform cartilage From the epigastric angle the disease penetrated the fascia of the linea alba and extended along the falciform ligament to reach the liver. It must be pointed out that Handley's cases were advanced



Fig 237 A small carcinoma embolus in the peripheral sinus of a lymph node

ones with extensive disease of the chest wall In cases in which we control the local disease we need not ordinarily fear this type of spread

Regional Lymph Node Metastases

At some point in its evolution breast carcinoma metastasizes through the lymphatic trunks which leap from the breast to the regional lymph nodes Figure 237 shows a small embolus in the peripheral sinus of a lymph node, where these emboli are first caught upon entering a node As the carcinoma infiltrates the node it blocks the flow of lymph through it, and finally breaks through its capsule

Very nearly half the cases had metastases in the central node group only. The other node groups were only rarely involved alone.

It is also worth while to analyze the sequence of involvement of the groups of nodes in our data, particularly for two of the groups, the interpectoral and the subclavicular nodes. It will be recalled from our discussion of the routes of lymphatic metastasis from the breast that the interpectoral nodes provide a

Table 42. Relative Frequency of Metastases in the Different Node Groups
(Pickren, Presbyterian Hospital)

Node group	63 cases with involved nodes				All 125 cases studied			
	Number of cases in which nodes were found	Number of cases with involved nodes	Per cent with involved nodes	Per cent of all cases with involved nodes (63)	Number of cases in which nodes were found	Number of cases with involved nodes	Per cent with involved nodes	Per cent of all cases (125)
1 Subclavicular	61	11	18.0	17.5	119	11	9.2	8.8
2 Axillary vein	63	25	40.0	40.0	125	25	20.0	20.0
3 Central	63	58	92.1	92.1	125	58	46.4	46.4
4 Scapular	56	12	21.4	19.0	108	12	11.1	9.6
5 Ext. mammary	34	2	5.9	3.2	69	2	2.9	1.6
6 Interpectoral	44	12	27.3	19.0	81	12	14.8	9.6
Any region	63	63	100.0	100.0	125	63	50.4	50.4

Table 43. Metastases in Single Node Groups
(Pickren, Presbyterian Hospital)

Region	Number of cases	Per cent of all 63 involved cases
1 Subclavicular	—	—
2 Axillary vein	—	—
3 Central	27	42.9
4 Scapular	1	1.6
5 External mammary	1	1.5
6 Interpectoral	1	1.6

separate pathway to the subclavicular nodes at the apex of the axilla, bypassing the main axillary lymph node groups. Table 44 shows the node groups involved in twelve cases in which there were metastases in the interpectoral nodes. In none of these cases was there metastasis solely via the interpectoral route as evidenced by metastases being found only in the interpectoral and the subclavicular nodes. Our data suggest, therefore, that when breast carcinoma metastasizes through the interpectoral route, the nodes of the main axillary route will be found to be involved.

of patients with not too extensive axillary node involvement are cured by radical mastectomy in which the axillary nodes, but none of the other regional lymph node groups, are removed

The cancerous emboli usually reach the central part of the axillary node filter first Our data show that the nodes of the central group are not only the group most often involved, but also the group most often exclusively involved The highest nodes in the filter, the subclavicular nodes, are the last to be involved, and have not, in our data, been alone involved I have been marking my operative specimens with silk threads placed at the most medial and the most lateral points of the axillary dissection for a long time, with the intention of making it possible for the pathologist to determine the site of metastasis in the axillary lymph node filter, as well as the number of nodes involved It has been only during the last few years, during which we have been clearing the axillary specimens in the laboratory of Surgical Pathology at the College of Physicians and Surgeons,

Table 41. Extent of Lymph Node Involvement within Each Group of Nodes

(Pickren, Presbyterian Hospital)

Node group	63 cases with involved nodes			All 125 cases studied		
	Number found	Number involved	Per cent involved	Number found	Number involved	Per cent involved
1 Subclavicular	238	32	13 4	435	32	7 4
2 Axillary vein	891	122	13 7	1644	122	7 4
3 Central	775	189	24 4	1401	189	13 5
4 Scapular	445	28	6 3	789	28	3 5
5 External mammary	89	2	2 2	176	2	1 1
6 Interpectoral	134	22	16 4	215	22	10 2
Total	*2573	*396	15 4	*4661	*396	8 5

* Total includes one case not assignable to node groups

however, that we have been able to determine the position of the metastases with satisfactory accuracy Tables 41 and 42 show these data from Pickren's recent series of 125 cleared axillary specimens studied in our laboratory

These data (Table 41) show first of all that the nodes of the central group, although not the most numerous, show a higher degree of involvement (24 4 per cent) when metastases are found in them, than any other node group

More significant is the fact that metastases are found more than twice as frequently (92 1 per cent) in the central node group as in any other node group (Table 42) This single fact confirms the great importance of this node group in the axillary lymph node filter The axillary vein group is a poor second in importance The scapular, interpectoral, and subclavicular node groups have a similar low incidence of metastases Involvement of the external mammary nodes is so infrequent that they cannot be regarded as of much importance

It is interesting to study the frequency of metastases in single node groups in these data, as shown in Table 43

Davis and Neis at the University of Nebraska studied the distribution of axillary lymph node metastases in 77 operative specimens of breast carcinoma They used the clearing technique and found an average of 31 4 nodes per case Unfortunately they used a different anatomical grouping of axillary lymph nodes from what I have used which makes comparison of our findings difficult.

Zeitlhofer in Vienna studied the anatomical distribution of lymph node metastases in the axilla in a series of 169 radical mastectomy specimens Since he did not, however use the clearing method his data do not bear comparison with Pickren s A similar study recently published by Berg has the same defect

Of the patients coming to the Presbyterian Hospital during the last generation with primary untreated carcinomas of the breast approximately 70 per cent have had axillary metastasis on admission I obtain this figure by adding to the patients in whom the presence of axillary metastasis was proved by operation those in whom there was clinical evidence of axillary metastasis on admission but since no operation was done, proof was lacking

The Influence of Social Status on the Incidence of Axillary Metastasis Of the various factors which influence the incidence of axillary metastasis the social status of the patient is one of the most important Private patients discover their breast carcinomas earlier and come more promptly for treatment, and as a result they are found to have axillary metastases less often than ward patients Taylor and Nathanson reported axillary metastases in only 47 per cent of private patients operated upon in the Massachusetts General Hospital while 65 per cent of the ward patients had axillary metastases.

Table 46. Incidence of Axillary Metastasis from Mammary Carcinoma by Social Status of Patient
(Presbyterian Hospital, 1915–1942)

Hospital status	Number of cases	Number with axillary metastasis	Per cent
Private	427	247	57 7
Ward	690	443	64 2
Total	1117	690	61 8

Our Presbyterian Hospital data, shown in Table 46 do not show as striking a difference between private and ward patients as the Massachusetts General Hospital data, but reveal a similar trend

The Influence of the Age of the Patient on the Incidence of Axillary Metastasis In keeping with the widely held belief that breast carcinoma is less malignant in old age we might expect the frequency of axillary metastasis to decrease with advancing age Taylor and Nathanson found this to be true in their data. They reported that in a group of their patients under the age of 46 axillary node involvement was found in 77 per cent, while in a group of patients over the age of 60 only 57 per cent had axillary node involvement

Our Presbyterian Hospital data bearing on this point, as shown in Table 47 fail to confirm this age relationship There is no statistically significant difference in the incidence of axillary metastases between the younger and older age groups.

The subclavicular nodes situated at the terminal inner end of the axillary filter were never involved in our cases (Table 45) unless there were metastases in the central, scapular, or axillary vein groups of nodes In all but one of the 11 cases with subclavicular metastases at least two of these more peripherally situ-

Table 44. 12 Cases of Interpectoral Node Involvement Showing the Involvement of Other Axillary Lymph Node Groups

(Pickren, Presbyterian Hospital)

Number of involved nodes found in various regions						Total involved	Total nodes found
S P No	Sub-clavicular	Axillary vein	Central	Scapular	Inter-pectoral		
A 29337					1	1	58
A 34614			1		1	2	34
A 28550			1		1	2	35
A 32451			3		2	5	59
A 34640			3		1	4	76
A 27955		3	3		1	7	32
A 34164		9	6		2	17	43
A 31377		1	4		2	7	44
A 29229		2	1	1	4	8	46
A 27972	1	11	7		1	20	39
A 30752	12	13	7	3	2	37	69
A 31458	1			1	4	6	48

Table 45 11 Cases of Subclavicular Node Involvement Showing the Involvement of Other Axillary Lymph Node Groups

(Pickren, Presbyterian Hospital)

Number of involved nodes found in various regions]							Total involved nodes	Total number of nodes found
S P No	Subcla-vicular	Axillary vein	Cen-tral	Sca-pular	External mam-mary	Inter-pectoral		
A 27368	3	1	2				6	51
A 31806	1	4	3				8	36
A 32203	2	10	6				18	33
A 34135	1	9	1				11	34
A 27108	1	3	10	2			16	41
A 28815	5	6	8	9			28	38
A 33353	1	3	4	1			9	45
A 31566	4	17	11	2	1		35	42
A 27972	1	11	7			1	20	39
A 30752	12	13	7	3		2	37	69
A 31458	1			1		4	6	48

ated node groups contained metastasis This confirms my conviction that the subclavicular nodes actually constitute the last line of defense in the axillary filter In general the patients in whom subclavicular metastases were found were hopelessly far advanced and incurable by surgery

What is more important is what these facts mean in terms of the hope of effective surgical attack The possibility of cure depends upon the absence of axillary lymph node metastases more than upon anything else If most patients with small primary carcinomas already have axillary metastases when they come for treatment we cannot have much hope of improving the results of operation by early diagnosis This pessimistic point of view is in fact one which several recent authors have presented Park and Lees estimated that 60 per cent of the patients have metastasis when their tumor first becomes palpable McKinnon has stated that axillary metastasis is found in practically all cases of typical breast cancer no matter how small the lesion

In reviewing these studies Gilliam has shown that a more sophisticated statistical approach might well produce different conclusions concerning the presence of metastasis in early stages of the disease He concluded that 30 per cent is a more reasonable figure than Park and Lees 60 per cent of axillary metastasis at onset of symptoms His main point is that no estimate of the proportions of highly malignant and less malignant tumors can be made from data now at hand without a considerable use of assumptions

Kraus has also reviewed Park and Lees studies and finds their analyses unconvincing

It is of course true that ideally we need to know precisely when a breast carcinoma originates, its exact size after a known interval of growth and just when it metastasizes, if we are to determine its malignancy But we can never hope to have these data and lacking them we can only do as best we can with what data are available The best way we have at present of answering the question of how early axillary metastases occur is to correlate the size of the primary breast carcinoma as measured in centimeters by a skilled clinician, or measurements of the operative specimen by the pathologist with the histological evidence of the presence of axillary metastases In our Presbyterian Hospital records we have careful clinical, as well as gross pathological measurements on approximately a thousand breast carcinomas Tumor size and incidence of axillary metastases are shown in Table 49 Carcinomas 1 cm or less had metastasized to the axilla in

Table 49 Incidence of Axillary Metastases by Size of Primary Carcinoma (Pathological Measurements)
(Presbyterian Hospital 1915–1942)

Size of primary carcinoma	Number of tumors	Number with axillary metastases	Per cent with axillary metastases
Under 11 mm.	42	17	40 5
11–19 mm.	103	60	58 3
20–29 mm.	237	130	54 9
30–49 mm.	322	200	62 1
50–69 mm.	160	117	73 1
70 and over	94	73	77 7
Total	958	597	62 3

only 40 per cent of the cases, while those 7 cm or more in diameter had metastasized in approximately 80 per cent.

Taylor and Nathanson, in discussing the higher incidence of axillary metastasis in their younger patients, sought an explanation for it in a greater frequency of more malignant undifferentiated carcinomas in their younger patients We have tested this explanation in our Presbyterian Hospital data and we are unable to confirm it Table 48 shows that well differentiated Grade I carcinomas were more frequent in our series of patients under the age of 45 than in our patients over the age of 60

Table 47. Incidence of Axillary Metastasis in 1135 Radical Mastectomies for Carcinoma by Age of Patient

(Presbyterian Hospital 1915–1942)

Age—Years	Number of cases	Number with *axillary* metastasis	Per cent with *axillary* metastasis
Under 30	24	15	62 5
30–34	50	28	56 0
35–39	112	75	67 0
40–44	194	128	66 0
45–49	196	120	61 2
50–54	179	106	59 2
55–59	138	82	59 4
60–64	106	70	66 0
65–69	65	37	56 9
70–74	31	18	58 1
75 and over	18	11	61 1
Total	1113	690	62 0

Table 48 Age Distribution of Mammary Carcinoma According to Microscopic Grade

(Presbyterian Hospital 1915–1942)

Age of patient	Number of patients	Grade I		Grade II & III	
		No	Per cent	No	Per cent
Under 45	379	36	9 5	343	90 5
60 and over	221	12	5 4	209	94 6

The Influence of the Size of the Primary Carcinoma on the Incidence of Axillary Metastases. In any series of patients with breast carcinoma there are some whose lesions are highly malignant and grow rapidly and metastasize to the axilla early Other patients have carcinomas of lesser malignancy that grow more slowly and metastasize late to the axilla Studies correlating the size of the primary carcinoma in the breast with the microscopical findings in the axillary nodes are the best available guide to the comparative frequency of carcinomas of these higher and lower degrees of malignancy For example, small carcinomas that have metastasized to the axilla can be classified as being highly malignant The proportion of such tumors in any body of data may be expressed as a percentage

Grades II and III which do not differ greatly from each other Unfortunately Grade I carcinomas constitute but a small proportion of all breast carcinomas

Table 52 shows the relationship of these grades of malignancy to the incidence of axillary metastases It is apparent that the Grade I carcinomas are not as likely to have metastasized as the Grade II and Grade III carcinomas

Table 52. The Incidence of Axillary Metastases by Pathological Grade of Primary Carcinoma
(Presbyterian Hospital 1915–1942)

Pathological grade	Number of tumors	Number with axillary metastases	Per cent with axillary metastases
I	84	32	38
II	422	257	61
III	597	395	66
Total	1103	684	62

Taylor and Nathanson reported a similar study of the relationship of pathological grade to the incidence of axillary metastases in the Massachusetts General Hospital Their results as shown in Table 53 emphasize even more than ours the lesser likelihood of axillary metastases in the Grade I carcinomas

Table 53. Grade of Malignancy and Axillary Metastases of Carcinoma of the Breast
(Taylor and Nathanson, Massachusetts General Hospital 1921–1932)

Grade	Total cases	Per cent metastases
I	71	14
II	329	64
III	205	81
Total	605	60

Extension to the Contralateral Axillary Nodes Occasionally metastases appear in the nodes of the opposite axilla. This phenomenon is usually seen late in the course of carcinoma when metastases have already developed elsewhere Handley found it in 6 per cent of 422 autopsies We have made a clinical diagnosis of contralateral metastases in about 4 per cent of our patients as shown in Table 54

Table 54 Contralateral Axillary Metastases
(Presbyterian Hospital 1935–1942)

Type of case	Number of cases	Number with contralateral breast metastases	Per cent
Primary non-operated cases	173	8	4 6
Primary operated cases	495	20	4 1
Total	668	28	4 2

Similar data, although based on smaller series of cases, have been published by Ackerman (Table 50) and by Eggers and his associates (Table 51)

These data relating the size of the primary carcinoma to the incidence of axillary metastases certainly indicate that the major proportion—between 60 and 70 per cent—of small carcinomas of the breast have not metastasized to the

Table 50. Incidence of Axillary Metastases by Size of Primary Carcinoma (Pathological Measurements)

(Ackerman, Barnes Hospital 1949–1952)

Size of primary carcinoma	Number of tumors	Number with axillary metastases	Per cent with axillary metastases
2 cm or below	61	21	34 4
2 to 3 cm	61	30	49 1
3 to 4 cm	39	23	58 9
4 to 6 cm	38	24	63 1
Over 6 cm	21	18	85 7
Diffuse	26	15	57 6
Not mentioned	23	12	52 1
Total	269	143	53 1

axilla when patients discover their disease Large carcinomas, on the other hand, have usually metastasized when the patient comes for treatment These facts are an unequivocal indication of the importance of detecting and treating breast carcinomas while they are yet small

Table 51 Incidence of Axillary Metastases by Size of Primary Carcinoma (Pathological Measurements)

(Eggers, New York Post-Graduate Hospital 1924–1933)

Size of primary carcinoma	Number of tumors	Number with axillary metastases	Per cent with axillary metastases
2 cm or below	40	11	27 5
2 to 3 cm	50	30	60 0
3 to 4 cm	35	24	68 5
4 to 6 cm	42	37	88 0
Over 6 cm	45	42	93 3
Not stated	66	52	78 7
Total	278	196	70 5

The Influence of the Pathological Grade of the Primary Carcinoma on the Incidence of Axillary Metastases The pathological grade of the individual mammary carcinoma is an exceedingly important factor in determining its capacity to metastasize I shall discuss the criteria that Dr Stout and I rely upon in grading breast carcinomas in Chapter 25, and for present purposes merely classify them in three grades Grade I is the most important of the three grades because the carcinomas that fall into it are much less malignant than those in

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Extension to the Contralateral Axillary Nodes Occasionally metastases appear in the nodes of the opposite axilla. This phenomenon is usually seen late in the course of carcinoma when metastases have already developed elsewhere Handley found it in 6 per cent of 422 autopsies We have made a clinical diagnosis of contralateral metastases in about 4 per cent of our patients, as shown in Table 54

Table 54 Contralateral Axillary Metastases
(Presbyterian Hospital 1935–1942)

Type of case	Number of cases	Number with contralateral breast metastases	Per cent
Primary non-operated cases	173	8	4 6
Primary operated cases	495	20	4 1
Total	668	28	4 2

It is of interest to speculate as to the lymphatic route by which the disease reaches the nodes in the opposite axilla If we assume that the route is by way of the lymphatics of the skin, the disease should reach and involve the opposite breast before it reaches the lymph nodes of the opposite axilla

In patients who have had radical mastectomy and have developed contralateral axillary node metastases we should, on the basis of this explanation, expect to find recurrence in the skin of the medial flap as well as disease in the opposite breast

But we have seen a number of patients with metastases in the nodes of the opposite axilla who did not have any evidence of regional skin recurrence, or of disease in the opposite breast The following case is an example

Miss A W , aged 71, had discovered a tumor in her right breast six weeks before I first saw her She had a 3 cm carcinoma of the upper outer sector of her right breast There were no palpable axillary nodes Radical mastectomy was done On microscopical study of the breast the carcinoma proved to be more extensive than clinical examination had suggested There were multicentric foci throughout the entire upper half of the breast Four of seventeen axillary nodes contained metastases

She was well until five and a half years later when she was found to have a 3 cm firm, movable, lower left axillary node There was no evidence of local recurrence of her previous right-sided carcinoma and no detectable distant metastases I could not make out anything abnormal in the left breast I excised the left axillary node On frozen section it was found to contain carcinoma I assumed that there must be an occult second primary carcinoma in the left breast and performed a left radical mastectomy

To our surprise, careful microscopical study of the left breast did not reveal carcinoma Six of the 41 left axillary nodes contained carcinoma, however The disease in these left axillary nodes closely resembled the carcinoma found in the right breast five and one-half years previously

Within three months after the second operation widespread local recurrence developed in the skin of the anterior chest wall, in the operative fields of both radical mastectomies She died while receiving irradiation fifteen months after her second operation

A case like this provides strong evidence that the carcinoma reached the nodes of the opposite axilla by embolism or permeation through the deep lymphatic fascial plexus beneath the opposite breast Emboli are swept through these deep lymphatics and reach the opposite axillary nodes before the disease has time to grow outward to invade the opposite breast

Internal Mammary Metastases

Halsted was perhaps the first to realize that breast carcinoma metastasizes to the internal mammary nodes, for he attacked mediastinal metastases surgically In 1898 he wrote "Dr H W Cushing, my house surgeon, has in three instances cleaned out the anterior mediastinum on one side for recurrent cancer It is likely, I think, that we shall in the near future remove the mediastinal contents at some of our primary operations " Halsted never mentioned the matter again What deterred him we can only guess

Sampson Handley, whose studies of the routes of spread of breast carcinoma in the early years of this century were an important contribution to our knowledge of the disease, became sufficiently convinced from his clinical experience

that metastasis takes place through the internal mammary route so that in 1922 he explored the mediastinum in 6 cases He found involved internal mammary nodes in 2 of them In 1927 Handley documented his belief in the importance of the internal mammary route of metastasis in a paper in which he described among others a remarkable case in which recurrences after radical mastectomy appeared at the inner ends of intercostal spaces, in one space after another from above downwards until death after twelve years In this paper Handley stated his belief that *by the time the axillary nodes are enlarged the internal mammary nodes are frequently and perhaps usually invaded*

The proof of this important rule has been provided by Sampson Handley s son Richard Handley Following his father as surgeon to the Middlesex Hospital he maintained an interest in the internal mammary route In 1946 he began to dissect out the node in the second interspace at the completion of radical mastectomy He shortly reported his findings in 5 cases The axillary nodes and the second internal mammary node were both found to be involved in 2, the internal mammary nodes only in 2, and neither axillary nor internal mammary nodes in the fifth case.

These results led Handley to adopt excision of the second or third internal mammary node as a routine at the completion of radical mastectomy As time went on and his data accumulated he often extended his exploration to more than one of the upper three interspaces, and recently he has begun to explore all three upper interspaces as a routine

Handley s latest report presents these data from 150 patients This is the largest consecutive series of cases of breast carcinoma with information concerning the status of the internal mammary nodes They are such important data that I quote from it in detail

Table 55. Regional Lymph Node Spread of Breast Cancer in Relation to Site of Primary Growth

(Table I—Handley and Thackray 1954)

Node Involvement	Site of primary growth: Center and inner half of breast	Site of primary growth: Outer half of breast	Total	Per cent
All nodes free	16	33	49	32 6
Axillary nodes only invaded	12	40	52	34 6
Internal mammary nodes only invaded	6	2	8	5 3
Both axillary and internal mammary nodes invaded	27	14	41	27 3
Total no of cases	61	89	150	

Table I shows that 33% of the primary growths in this series had metastasized to the internal mammary chain at the time of operation If the 61 growths in the medial half of the breast (with which are included the tumours behind the nipple) are considered, 33 (54%) of them had metastasized to the chain 6 of them to the chain alone, whereas only 16 of the 89 growths (18%) in the lateral half of the

breast had metastasized to the chain, and 2 to the chain alone Table II shows a further breakdown by quadrant, and it is of particular interest that 16 of the 17 growths in the region of the nipple had metastasized to lymph nodes, in 12 the internal mammary chain being invaded "

Table 56 Regional Lymph Node Spread of Breast Cancer in Relation to Site of Primary Growth by Quadrant
(Table II—Handley and Thackray, 1954)

Node involvement	Site in breast by quadrants: Upper inner	Lower inner	Central	Upper outer	Lower outer	Total
All nodes free	11	4	1	28	5	49
Axillary nodes only invaded	6	2	4	34	6	52
Internal mammary nodes only invaded	4	0	2	2	0	8
Both axillary and internal mammary nodes invaded	10	7	10	13	1	41
Total	31	13	17	77	12	150

"If only the tumours which had already metastasized to the axilla are considered, 41 of the 93 cases (44%) had metastasized to the internal mammary chain Of the 39 cases in which a tumour in the inner half of the breast had metastasized to the axilla, the internal mammary chain was invaded in 27 (69%) Even with tumours in the outer half of the breast, if the axilla was invaded 14 of the 54 cases (26%) had internal mammary deposits

Table 57 Relation of Degree of Axillary Involvement to Internal Mammary Invasion
(Table III—Handley and Thackray, 1954)

Extent of axillary invasion	Number of cases	Cases with internal mammary invasion
0 (free)	57	8 (14%)
1 (light)	23	6 (26%)
2 (moderate)	32	12 (37%)
3 (heavy)	34	22 (65%)

"An attempt was made to see whether the degree of anatomical invasion of the axilla bore any relation to the frequency of internal mammary deposits There were 146 cases in which the data enabled a rough estimate to be made of the anatomical degree of axillary involvement, and four degrees, from 0 to 3, were somewhat arbitrarily fixed by the clinical state of the patient, the number of invaded lymph nodes sectioned, and whether or not the apical axillary nodes were involved

"Table III gives the results, and it shows what one might expect—namely, that the greater the degree of axillary involvement the more likely is it that the

internal mammary chain will be invaded—but it disposes of the argument that only after the axillary lymphatics are completely choked is the chain invaded

Hutchinson in Seattle was stimulated by Handley s original 1947 report He began in 1949 to excise the internal mammary nodes in the upper three interspaces at the conclusion of his radical mastectomy His 1953 report presents his findings in 81 consecutive private cases His data shown in Table 58 are very like Handley s

Table 58. Carcinoma of the Breast Regional Lymph Node Metastases
(Hutchinson 1949–1951)

Extent of metastasis	Site of primary carcinoma		Total cases	
	Central and inner half	Outer half	No.	Per cent
All nodes free	14	24	38	46 9
Axillary nodes only involved	2	20	22	27 2
Internal mammary nodes only involved	1	1	2	2 5
Both axillary and internal mammary nodes involved	3	16	19	23 4
Total	20	61	81	

There are two features of Hutchinson s cases that differ from Handley s cases In Hutchinson s private cases the disease was, as would be expected, less advanced and lymph node metastases in general less frequent A second, and most important point for future study is the comparative frequency of internal mammary metastases from the inner and outer halves of the breast. Hutchinson s data do not show as did Handley s a much greater likelihood of internal mammary metastases from carcinomas of the center and medial half of the breast.

Margottini and Bucalossi in Italy became interested in Handley's work, and in 1948 began to excise the internal mammary nodes at the completion of radical mastectomy Their excision was a more thorough one in that they removed the medial 2 cm of the second and third costal cartilages thus laying bare the internal mammary blood vessels and the accompanying lymphatic chain with its nodes, in the upper three interspaces They then ligated the vessels as high as possible in the first interspace, and as low as possible in the third interspace and excised all of these tissues extrapleurally

In a series of 110 of these operations done in Rome and Milan, Margottini and his associate Bucalossi reported their findings as shown in Table 59

Their data should give a more accurate picture of internal mammary metastasis than either Handley s or Hutchinson s because they removed the entire internal mammary chain in continuity in the upper three interspaces The data do not show a higher incidence of internal mammary metastases from carcinoma of the inner half than from that of the outer half of the breast.

Giacomelli and Veronesi in 1952 published another report of the internal mammary dissections carried out at the National Cancer Institute in Milan during 1948 to 1950 Of the 90 cases that they referred to 49 had been included in Margot

breast had metastasized to the chain, and 2 to the chain alone Table II shows a further breakdown by quadrant, and it is of particular interest that 16 of the 17 growths in the region of the nipple had metastasized to lymph nodes, in 12 the internal mammary chain being invaded "

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"Table III gives the results, and it shows what one might expect—namely, that the greater the degree of axillary involvement the more likely is it that the

by means of gauze strips to expose the internal mammary artery and veins and lymph nodes These vessels and the accompanying lymphatics and nodes together with surrounding fatty tissue were then excised extrapleurally from beneath the first cartilage down to the level of the fifth cartilage This was the first investigation of regional lymph node metastasis in breast carcinoma that provided data regarding the relative frequency of axillary supraclavicular and internal mammary metastases The series was made up of comparatively favorable cases, for the axillary nodes contained metastases in only 43 per cent of the patients The supraclavicular nodes were found to be involved in only 5 3 per cent, and the internal mammary nodes in only 29 per cent of the patients If only the patients with axillary metastases were considered 9 per cent had supraclavicular metastases and 52 per cent internal mammary metastases Unfortunately Dahl Iversen did not include in his report of this series a detailed statement of the frequency of internal mammary metastases in relation to the site of the carcinoma in the breast

In a *fourth* series of 100 patients reported in 1954 Dahl Iversen also combined excision of the supraclavicular and internal mammary nodes with radical mastectomy This series was likewise composed of remarkably favorable cases for only 41 per cent were found to have axillary metastases

In order to learn as much as possible regarding the relationship of the frequency of internal mammary metastases to the site of the carcinoma in the breast in Dahl Iversen s studies, I have combined his findings in his second and fourth series of cases into a single Table 61

Table 61 Carcinoma of Breast Regional Lymph Node Metastases
(Andreassen, Dahl Iversen and Soerensen, 2nd and 4th Series)

Extent of metastasis	Site of primary carcinoma		Total cases	
	Medial	Lateral	No.	Per cent
All nodes free	31	48	79	51 6
Axillary nodes only involved	7	37	44	28 8
Int. mammary only involved	8	—	8	5 2
Axillary and int. mammary involved	11	8	19	12 4
Axillary and supraclavicular involved	—	3	3	2 0
Total	57	96	153	100 0

The incidence of internal mammary metastases in the total of 153 patients was 17 6 per cent. Thirty three per cent of those with carcinoma of the medial half of the breast had internal mammary metastases, while only 8 3 per cent of those with carcinoma of the lateral half had internal mammary metastases

Like others whose data I have presented I was myself stimulated by Richard Handley to investigate the internal mammary route of metastasis. Since I had been interested for many years in the problem of the proper selection of patients for operation, it was only reasonable that I should bring the new knowledge of the internal mammary route to bear on this question I therefore began in 1951 to excise the internal mammary nodes not as a part of radical mastectomy but

tini's earlier report The findings in the cases included in this series closely approximate those in the earlier series Giacomelli and Veronesi included, however, an interesting table (Table 60) reproduced below, which relates the size of the primary carcinoma in the breast to the frequency of internal mammary metastases It is obvious that the larger the carcinoma the more likely internal mammary metastases

Table 59 Carcinoma of Breast; Regional Lymph Node Metastases
(Margottini and Bucalossi, 1948–1949)

Extent of metastases	Site of primary carcinoma			Total cases	
	Inner half	Outer half	Entire breast	Number	Per cent
All nodes free	20	21	0	41	37 3
Axillary nodes only involved	18	25	1	44	40
Internal mammary nodes only involved	0	2	0	2	1 8
Both axillary and internal mammary nodes involved	9	11	3	23	20 9
Total	47	59	4	110	

Table 60 The Size of the Primary Breast Carcinoma Related to the Incidence of Internal Mammary Metastases
(Giacomelli and Veronesi, 1948–1950)

Size of primary carcinoma	Number cases	Without metastases	Axillary met only	Int mam met only	Axil and int mam met	Per cent int mam metastases
Less than 10 cm	35	12	17	1	5	17
10–30 cm	45	16	16	0	13	29
30 cm or more	10	11	3	0	6	60
Total	90	39	36	1	24	27 7

In Copenhagen, Dahl-Iversen began to investigate the frequency of regional node metastasis in breast carcinoma In his *first* series of 98 cases, studied during 1949, he performed a supraclavicular lymph node dissection in addition to radical mastectomy

In 1951 he extended his studies to include the internal mammary nodes He excised the internal mammary nodes in the upper three interspaces in a series of 57 patients in whom he also performed radical mastectomy The nodes were excised from each interspace separately as Handley had done, without cutting the costal cartilages This group of 57 patients constituted a *second* series for Dahl-Iversen

In a *third* series of 76 patients, treated during 1951 and 1952, Dahl-Iversen and his associates excised the supraclavicular, as well as the internal mammary nodes, at radical mastectomy A more thorough method of excising the internal mammary nodes was used The second, third, and fourth costal cartilages were cut across about 1 cm from the sternal border, and the wall of the thorax elevated

All that I have written above regarding internal mammary metastasis has implied spread of the carcinoma in a cephalad direction along the internal mammary lymphatic trunk through the upper three interspaces to the grand central lymphatic terminal at the base of the neck It must not be forgotten however, that when the upper internal mammary nodes are blocked by metastasis the



Fig. 238 The inner aspect of the sternum showing metastases in the upper four inter spaces from carcinoma of the breast.

disease may extend downward in a retrograde manner to the prepericardial lymph nodes on the surface of the liver from which the internal mammary trunk lymphatics originate This is certainly the route by which carcinoma of the breast reaches the liver in some patients

Internal mammary metastases do not, in most patients, reach a large size even in the terminal stage of breast carcinoma, when there are massive metastases in the lungs liver or elsewhere Figure 238 shows the inner aspect of the sternum

as a preliminary biopsy procedure for the purpose of investigating internal mammary spread of carcinoma. I combined the biopsy of the primary tumor in the breast with excision of the supraclavicular nodes and the internal mammary nodes in the first, second and third interspaces Each interspace was explored in turn through an incision along the sternal edge This so-called *triple biopsy* was a preliminary operative procedure to establish the presence of carcinoma and the extent of the regional lymph node metastasis By adding this biopsy information to the criteria of operability that Dr Stout and I had worked out, we were able to substitute pathological for clinical evidence regarding the extent of regional lymph node metastasis and to make our selection of cases for operation more accurate

Our data regarding internal mammary metastasis is now extensive, for we have biopsied one or more of the interspaces, or excised the internal mammary chain with the chest wall, in a total of 304 patients Our data suffer from several handicaps, however In the first place they are not derived from a consecutive series of cases as Handley's We have been able to investigate the status of the internal mammary nodes in most of the patients admitted with breast carcinoma to the Francis Delafield Hospital, but these patients, in general, have had more advanced disease than our Presbyterian Hospital patients, particularly those on the private service In the Presbyterian Hospital, because of limitations of operating room time and economic restrictions, we have had to limit our internal mammary biopsies to those patients whose tumors are situated in the inner half of the breast or its central area, to those whose tumors are locally advanced, and to those who have clinically involved axillary nodes Our data from the Presbyterian Hospital therefore indicate what may be expected in the internal mammary nodes in advanced, not in early, breast carcinoma Finally, since we have used the finding of supraclavicular and/or internal mammary metastases as a contraindication to radical mastectomy, patients with these metastases have not had axillary dissection and we are unable to present data correlating the findings in the internal mammary nodes with the status of the axillary nodes

Subject to these limitations, our data relating the occurrence of internal mammary metastases to the site of the primary carcinoma in the breast are shown in Table 62 They confirm the greater likelihood of internal mammary metastases when carcinoma is situated in the central or the inner portion of the breast

Table 62 Carcinoma of the Breast, Internal Mammary Biopsies
(Presbyterian and Francis Delafield Hospitals, 1951–1955)

Result of biopsy	Central and inner half of breast		Outer half of breast		Total cases	
	No	Per cent	No	Per cent	No	Per cent
No internal mammary metastases	99	61 1	109	76 8	208	68 4
Internal mammary metastases	63	38 9	33	23 2	96	31 6
Total	162	100 0	142	100 0	304	100 0

in Figure 241 In other cases minute carcinoma emboli consisting of only a few cells have been found in only one section of a number cut through a small node Figure 242 shows the only microscopical section that contained carcinoma among six cut from three levels through a 5 mm node removed from the first interspace of a patient with a 5 cm carcinoma of the lower outer sector of the breast. The minute embolus of carcinoma cells is caught in the afferent lymphatic as it enters the peripheral lymphatic sinus of the node In searching for and

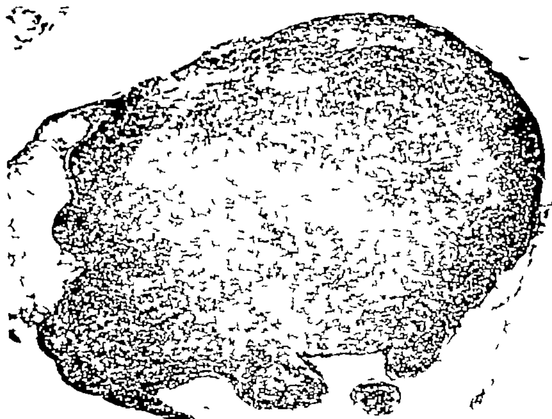


Fig 240 A 5 mm. internal mammary node, one third of which is replaced by metastatic carcinoma

demonstrating such minute foci of carcinoma we have entered, both surgically and pathologically into a new order of smallness of size Minute though such internal mammary metastases may be they kill the patient if they are not detected and treated

These recent studies of the internal mammary route in breast carcinoma suggest the following conclusions

1 Before metastasis to the axillary nodes occurs, internal mammary node involvement is so infrequent that it has little therapeutic significance

2 After metastasis to the axillary nodes has occurred, involvement of the internal mammary nodes in the upper three interspaces may be expected in between 30 and 50 per cent of cases

3 Metastases to the internal mammary nodes are more frequent from carcinomas in the inner half and central region of the breast than from those in the outer half of the breast

4 These internal mammary node metastases are often of minute size In order to find them, all of the areolar tissue, as well as any grossly evident lymph nodes,

and costal cartilages in such a case Enlarged nodes containing metastases, and measuring about 1 cm in diameter, are seen in the upper four interspaces

In occasional patients, metastases to the internal mammary nodes grow vigorously enough to form a parasternal mass which is obvious clinically In such patients the external mass represents the outward extension through the interspace of what was originally a minute carcinomatous embolus in one of the internal mammary nodes Figure 239 shows this kind of parasternal metastasis developing over the second right interspace in one of our patients three years after she had had a so-called radical mastectomy performed at another hospital

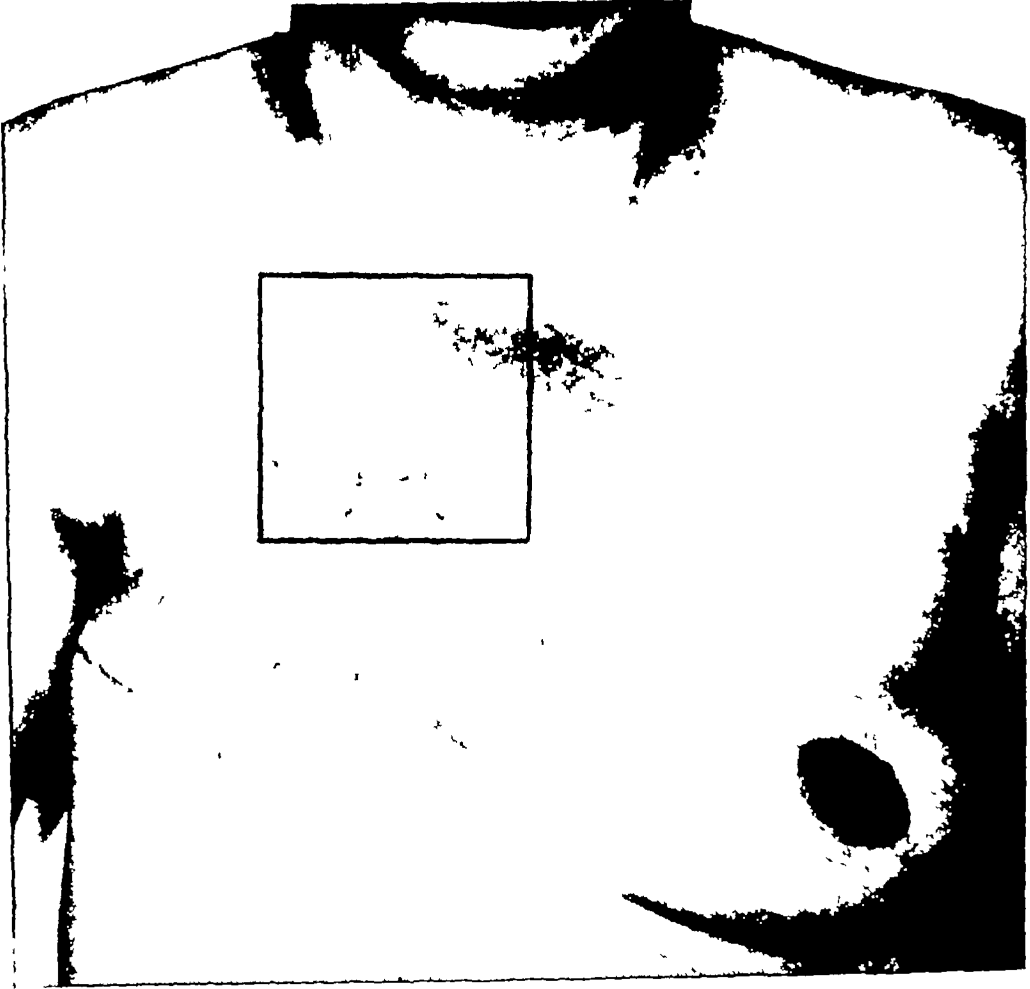


Fig 239 Internal mammary metastasis from carcinoma of the breast appearing externally as a mound-like tumor over the second interspace at the sternal edge

The parasternal tumor forms a mound-like, firm, poorly delimited mass, solidly fixed to the chest wall, over which the skin is slightly reddened

In the patients with breast carcinoma at an earlier stage in whom we dissect out the internal mammary nodes as part of our biopsy procedure to determine the extent of the disease, our chief difficulty arises, indeed, from the minute size of the nodes Figure 240 shows a typical internal mammary node 5 mm in diameter containing metastasis We have, however, found metastases in nodes that did not measure more than 1 or 2 mm in diameter We have also, in a number of instances, removed internal mammary nodes and found no metastases in them, but found minute foci of carcinoma in the adjacent areolar tissue We have also found the disease in small vessels removed in the dissection, as pictured

the apex of the axilla along the subclavian vein to nodes situated upon its confluence with the internal jugular vein behind the clavicle at the base of the neck Not long after he began to perform his epoch making radical mastectomy he added to it excision of the supraclavicular nodes He tried a variety of techniques that would permit stripping the infra and supraclavicular portions of the subclavian vein clean of all lymph nodes and fat He at first divided the clavicle but later found this unnecessary In 1898 he wrote the supraclavicular region is almost invariably cleaned out By 1907 when he reported his end results before the American Surgical Association he had performed supraclavicular dissection as part of radical mastectomy in a total of 101 cases He had also done the opera



Fig 242. Embolus of mammary carcinoma in afferent lymphatic of internal mammary lymph node from first interspace.

tion secondarily in 18 patients In 44 of these 119 patients the supraclavicular nodes had been found to be involved Yet only 2 of the 44 had been cured for five years or more

The poor results of supraclavicular dissection led Halsted s pupils to abandon it. It added a good deal of work to an operation that Halsted himself characterized as a very great labor and the number of cures attributed to it was very small. With the abandonment by most surgeons of the attack upon supraclavicular metastases, the importance of the supraclavicular route has been lost sight of until very recently

We owe the current revival of emphasis upon supraclavicular metastasis to Dahl Iversen of Copenhagen In 1949 he pointed out that supraclavicular lymph node recurrence was a very frequent type of recurrence in patients who developed

should be meticulously excised from the upper three interspaces This tissue should be sectioned in numerous levels and studied with great care

It would be a great advantage in determining treatment if these studies of internal mammary metastases permitted us to draw more exact conclusions as to the relationship of the frequency of internal mammary metastases to the site of the carcinoma in the breast Unfortunately they do not I have emphasized in

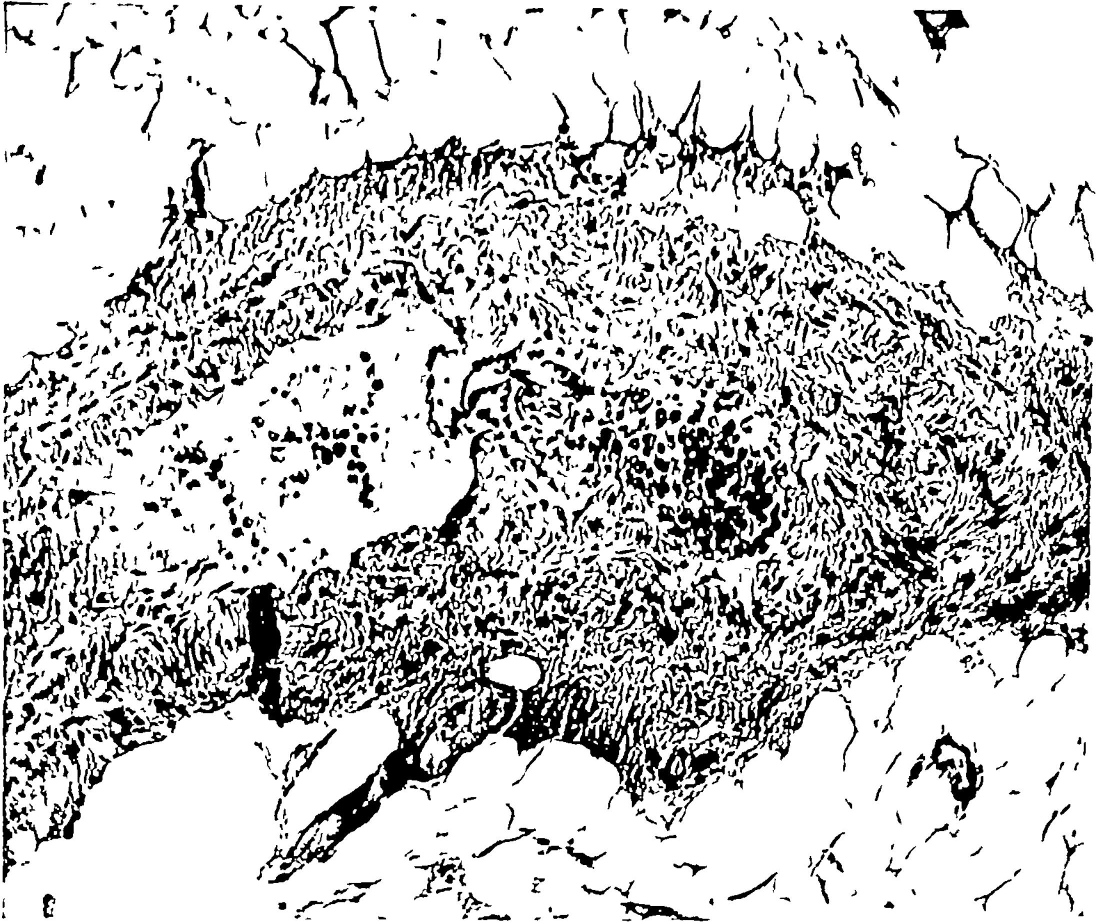


Fig 241 Metastatic mammary carcinoma in a small blood vessel excised during internal mammary biopsy

Chapter 5 the desirability of defining the site of the tumor in the breast in terms of seven specific zones The data I have presented here refer to the site of the tumor only in general terms as "inner," "outer" or "central " We cannot determine from such data whether or not carcinomas situated in the parasternal zones D and E, as I have defined them, are more apt to metastasize to the internal mammary nodes than carcinomas situated in the lower and upper inner sectors of the breast, zones C and F Such questions cannot be answered until additional specific data are available I have, however, some suggestive evidence based upon the frequency of parasternal metastases diagnosed clinically in my patients treated by radical mastectomy, which will be presented in Chapter 27

Supraclavicular Lymph Node Metastases

Halsted, again, was the pioneer in appreciating the frequency of supraclavicular lymph node metastasis He knew that the route of metastasis was from

Margottini in 1948 reported finding occult supraclavicular metastases in 23 6 per cent of a series of 75 patients in whom radical mastectomy had proved the existence of axillary metastases Margottini performed his prophylactic supraclavicular dissection as a separate stage two weeks after radical mastectomy

As I have already indicated in discussing internal mammary metastases I began in 1951 to carry out supraclavicular dissection as part of a triple biopsy procedure intended to determine operability Our cases do not form a consecutive series and they represent comparatively advanced disease The data that we have accumulated are shown in Table 65

Table 65. Results of Supraclavicular Node Biopsies
(Presbyterian and Francis Delafield Hospitals 1951–1955)

Extent of metastases	Number of cases	Per cent
Supraclavicular nodes involved no internal mammary node biopsy	4	3 6
Supraclavicular nodes involved internal mammary nodes free	2	1 8
Supraclavicular nodes involved internal mammary nodes also involved	17	15 6
Supraclavicular nodes free internal mammary nodes involved	15	13 6
Supraclavicular nodes free internal mammary nodes also free	69	62 7
Supraclavicular nodes free no internal mammary node biopsy	3	2 7
	110	100 0

From these data regarding supraclavicular metastases we can draw the following conclusions

1 Supraclavicular metastases are found only in patients in whom axillary metastases exist

2 In these patients with axillary metastases the incidence of metastases to the supraclavicular nodes is lower than the incidence of metastases to the internal mammary nodes Supraclavicular involvement occurs therefore, at a later stage than internal mammary involvement.

Metastasis to the Nodes at the Apex of the Axilla

It has been my experience that the supraclavicular nodes are in some cases still free of metastases although the disease has involved all the axillary nodes, or the highest axillary nodes

A patient with such extensive axillary metastases has, in my experience, an exceedingly small chance of cure by surgery I believe that radiotherapy is a better method of treatment for such patients. Dissection of the supraclavicular nodes for biopsy will fail under these circumstances to save the patient from futile radical mastectomy

In search of a more critical biopsy method of determining the extent of metastatic spread along the axillary-supraclavicular route, I began, early in 1955 to

recurrence following the conventional radical mastectomy He tabulated its frequency in several case series as shown in Table 63

Table 63 Frequency of Supraclavicular Recurrence Among Patients with Recurrence Following Radical Mastectomy

Author	Year	Number of cases with recurrent carcinoma	Per cent with supraclavicular recurrence
Dahl-Iversen	1927	48	27
Todd & Dawson	1937	107	24
Haagensen & Stout	1943	98	25
Roden	1944	139	21
Ducuing, Tailhefer and Baclesse	1947	257	22

It was such data as these that led Dahl-Iversen and his associates in 1947 to begin to dissect out the supraclavicular nodes as part of radical mastectomy Their first series consisted of 98 consecutive cases operated upon during 1947 and 1948 None of these patients had palpable supraclavicular nodes, but in 17 per cent metastases were found in the nodes removed by the dissection These supraclavicular metastases were found exclusively among the 51 patients who had axillary metastases, the incidence of supraclavicular metastasis in this group was therefore 33 per cent

Dahl-Iversen and his associates have subsequently carried out supraclavicular dissection in two additional series of patients on whom they performed radical mastectomy (their third series and their fourth series) These two more recent series of cases included 176 additional patients In these two series the incidence

Table 64 Supraclavicular and Axillary Metastases (Dahl-Iversen's 1st, 3rd, and 4th Series)

Extent of metastases	Number of cases	Per cent
Both axillary and supraclavicular nodes free	149	54 4
Axillary nodes involved but not supraclavicular	102	37 2
Supraclavicular nodes involved but not axillary	0	0 0
Both axillary and supraclavicular nodes involved	23	8 4
Total	274	100 0

of supraclavicular metastases was much lower than in the first series of cases supraclavicular metastases were found in only 8 per cent of the patients with axillary metastases The explanation for the lower incidence of supraclavicular metastases in Dahl-Iversen's more recent case series is to be found in the comparatively favorable nature of his recent clinical material The incidence of axillary metastases in his last two case series was only 42 per cent In contrast the incidence of axillary metastases in the latest Presbyterian Hospital series reported by Stout and myself was 61 6 per cent

Dahl-Iversen's data regarding supraclavicular metastases in his several series of cases are combined in Table 64

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From these data regarding supraclavicular metastases we can draw the following conclusions

1 Supraclavicular metastases are found only in patients in whom axillary metastases exist

2 In these patients with axillary metastases the incidence of metastases to the supraclavicular nodes is lower than the incidence of metastases to the internal mammary nodes Supraclavicular involvement occurs, therefore, at a later stage than internal mammary involvement

Metastasis to the Nodes at the Apex of the Axilla

It has been my experience that the supraclavicular nodes are in some cases still free of metastases although the disease has involved all the axillary nodes, or the highest axillary nodes

A patient with such extensive axillary metastases has, in my experience, an exceedingly small chance of cure by surgery I believe that radiotherapy is a better method of treatment for such patients Dissection of the supraclavicular nodes for biopsy will fail under these circumstances to save the patient from futile radical *mastectomy*

In search of a more critical biopsy method of determining the extent of metastatic spread along the axillary supraclavicular route, I began early in 1955 to

biopsy the apex of the axilla rather than the supraclavicular region In this axillary apex biopsy the nodes lying upon the most medial part of the axillary vein, between the origin of its thoraco-acromial axis branch and the point at which the vein passes beneath the tendon of the subclavius muscle, are removed Although we have not been doing these apex of axilla biopsies for very long we have already found metastases in this region in a number of patients, and have saved them from what I believe to be futile radical mastectomy Figure 243 shows metastatic



Fig 243 Biopsy from the apex of the axilla showing metastatic mammary carcinoma infiltrating fat

carcinoma infiltrating the fat at the apex of the axilla in a patient in whose axilla the only palpable evidence of disease was a 0 5 firm freely movable node

To date a total of 41 apex of axilla biopsies have been done, all but two as part of the triple biopsy routine In Table 66 the results of our axillary apex and supra-

Table 66 Axillary Apex Compared with Supraclavicular Biopsy in Triple Biopsies (Presbyterian and Francis Delafield Hospitals)

Extent of metastases	Supraclavicular and internal mammary regions biopsied	Apex of axilla and internal mammary regions biopsied
Total number of triple biopsies	103	39
Number with metastasis—any node group	34	13
Number with involved internal mammary nodes	32	10
Number with involved supraclavicular nodes	19	—
Number with involved nodes at apex of axilla	—	10

clavicular biopsies are compared It will be seen from this table that the incidence of metastases to the axillary apex nodes is higher than the incidence of supra clavicular metastases I believe that axillary apex biopsy is a more critical and a better guide than supraclavicular biopsy for the selection of patients for opera tion

Distant Metastases Through the Blood Stream

When breast carcinoma reaches the grand central lymphatic terminus at either side of the base of the neck carcinoma emboli are emptied directly into the left or right innominate vein from which they are carried through the right heart to the lungs

Emboli that break loose from carcinoma that has grown into veins in the breast are swept in the venous stream either to the internal mammary veins or to the axillary veins Both these sets of veins lead to the innominate veins the superior vena cava and the lungs A third venous route to the lungs is through the intercostal veins which empty posteriorly into the azygos veins, which in turn terminate in the superior vena cava These several routes by which carcinoma emboli reach the lungs are shown diagrammatically in Figure 23 in Chapter 1

In view of the opportunity for carcinoma emboli to reach the lungs that these venous routes provide it is not surprising that metastases to the lungs are very frequent in breast carcinoma They are in fact the most frequent form of distant metastasis, being found in from 60 to 65 per cent of all autopsies in cases of mam mary carcinoma Table 67 shows the comparative frequency of distant metastases of breast carcinoma to various organs as indicated in modern investigations I have not included in this table the much quoted antiquated 19th century data presented by Gross Török Paget Lazarus Barlow etc These old data largely based on gross pathology cannot compare in accuracy with modern meticulous histological studies I have included our data from the Delafield Hospital tabu lated by Sproul but not previously published

Lung Metastases

The carcinoma emboli that reach the lung through the right heart and the pulmonary arteries are caught and form tumor thrombi in the small arterial branches or in the capillaries They are too large to filter through the pulmonary capillary network Schmidt who wrote a classical description of the process of pulmonary metastasis thought that some of the carcinoma emboli that reach the lungs are choked and destroyed by the fibrosis that develops around them Walther agrees with this opinion He believes that latent lung metastases appear ing in some cases a number of years after successful mastectomy evolve from emboli that have remained locked up in fibrosed tumor thrombi in the lungs Certainly many carcinoma emboli that reach the lungs survive and grow vigor ously They form the rounded tumor nodules that are so often seen grossly at autopsy The roentgenologists call this the *nodular* form of pulmonary metastasis Figure 244 shows a characteristic roentgenogram of this type of metastasis with numerous round masses of varying size scattered throughout both lung fields

In rare cases only a single metastatic nodule is seen It presumably repre sents the only carcinoma embolus that has reached the lung for the patient

Table 67. Most Frequent Sites of Distant Metastases from Carcinoma of Breast at Autopsy

Organ	Kitain 1922 41 cases	Warren and Witham 1933 160 cases	Turner and Jaffe 1940 105 cases	Saphir and Parker 1941 43 cases	Walther 1948 186 cases	Abrams 1950 167 cases	Sproul Delafield Hospital 1955 100 cases
Lungs	54%	59%	62%	65%	62%	77%	69%
Liver	63%	58%		56%	35%	61%	65%
Adrenals	27%	31%		41%	8%	54%	49%
Kidneys	17%			14%	9%	13%	17%
Spleen	7%	14%		23%	3%	17%	17%
Pancreas	7%			11%	3%	14%	17%
Ovaries	17%	9%		16%	4%	23%	20%
Brain	9%			9%	6%	29%	22%
Thyroid					8%	5%	24%
Heart						8%	11%
Diaphragm				14%		25%	11%
Pericardium	5%			21%		35%	19%
Pleura	63%	37%		23%		65%	51%
Intestine							18%
Peritoneum	19%	12%		9%		25%	13%
Uterus							15%
Mediastinal lymph nodes				32%		66%	
Peritoneal lymph nodes		72%		26%		44%	76%
Retroperit lymph nodes				32%			
Inguinal lymph nodes				7%		2%	
Bones	56%	44%	57%		47%	73%	71%
Skin		39%		7%	1%	19%	30%
No metastases	2%	5%		7%	12%		2%

has no evidence of other distant metastasis and is cured by pneumonectomy

The following is a summary of one of the two cases of this kind that I have observed

Mrs. D B a widowed woman lawyer aged 54 consulted me July 25 1945 for a tumor of her right breast that she had first discovered in February Examination showed a hard poorly delimited tumor measuring 3 cm in diameter at the medial end of the inframammary fold of the right breast Like all carcinomas of the inframammary fold that I have studied it was fixed to the underlying chest wall Pectoral contraction brought out a definite notch in the contour of the breast in the vicinity of the tumor



Fig. 244 The roentgenographic appearance of the nodular type of bilateral pulmonary metastasis from mammary carcinoma.

A chain of 1 cm movable nodes was palpated in the right axilla. Skeletal and chest roentgenograms showed no evidence of metastasis.

After biopsy to prove the carcinomatous nature of the tumor radical mastectomy with the customary skin graft was done Twenty-two axillary lymph nodes were found in the specimen None contained metastasis.

The patient had no further evidence of disease until three and one-half years later when, in January 1949 a routine chest film showed a single well rounded density 2 cm in diameter in the lower posterior portion of the upper lobe of her right lung. She had no symptoms whatever and we failed to persuade her to permit thoracotomy until eight months later when new roentgenograms (Fig. 245) showed that the lung nodule had increased in size When the chest was opened October 26 1949 by Dr Richmond Moore, the only tumor nodule that could be found was the one seen in the x ray films.

Fig 245 Solitary pulmonary metastasis from mammary carcinoma as seen roentgenographically

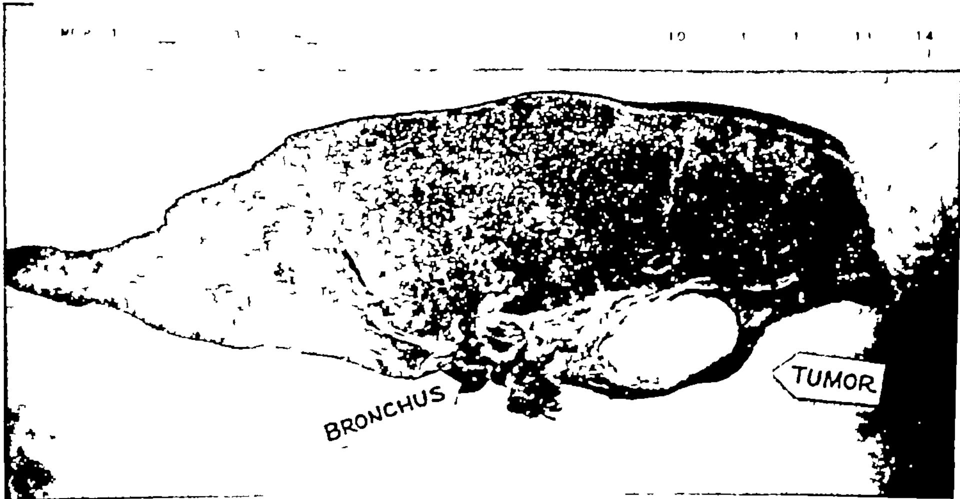


Fig 246 The gross appearance of the solitary pulmonary metastasis in the resected lung

It was a rounded 3 cm mass covered by normal visceral pleura and projecting slightly from the surface of the lower posterior portion of the upper lobe Right upper lobectomy was done The gross appearance of the resected lobe is shown in Figure 246 Microscopically the tumor was carcinoma similar to the primary breast carcinoma removed four years and three months previously The patient was well when last heard from in December 1955

Seiler and his associates collected reports of solitary metastasis to the lung treated by resection This was successful in a number of patients but none of them had had breast carcinoma

The usual course of events when carcinoma emboli reach the lung is quite different The emboli are numerous and in the process of their expanding and infiltrating growth they break through the walls of the small pulmonary arteries or capillaries in which they have lodged The disease then invades the structure of the lung diffusely filling up the alveoli blocking and permeating lymphatics and growing into the pulmonary veins Tumor fragments that break loose within the involved pulmonary veins are carried off back to the left heart and become carcinoma emboli in the systemic arterial circulation that carries them throughout the body The viscera with a rich blood supply like the liver spleen and adrenals, and certain bones such as the vertebrae are the most frequently involved It was formerly thought that metastases to the spleen were significantly infrequent but modern studies of this question show the spleen to be involved approximately as often as organs with a similar blood supply

It follows from this concept of the process of blood stream metastasis that involvement of the lungs always precedes the development of blood borne metastases in other parts of the body (an exception must be made for bone metastasis through the vertebral venous route which I shall discuss separately) Our clinical and autopsy evidence supports this premise It must of course be understood that pulmonary metastases are not infrequently too small to be seen grossly or roentgenographically and are found only by careful microscopical study of the lungs

The nodular type of lung metastasis is remarkably silent clinically If the parenchymal nodules are not associated with pleural involvement they produce no symptoms for months after they are first visible roentgenographically Only when they have grown to a relatively large bulk do they begin to produce cough and some degree of dyspnea With this type of pulmonary metastasis the respiratory symptoms are usually not the predominant ones in the terminal stage of the disease

There is however another type of pulmonary metastasis of breast carcinoma that does produce important respiratory symptoms It is the so-called lymphangitic type characterized by permeation of the lymphatics and obliterative fibrosis around tumor thrombi in the small arteries of the lungs This type of pulmonary metastasis is most often seen with carcinoma of the stomach but we have seen it several times in patients with breast carcinoma at the Delafield Hospital The most prominent symptom in these patients is dyspnea which rapidly increases It is accompanied by a productive cough chest pain and cyanosis The patients fail rapidly and die with terminal edema of the lungs and pneumonitis

Roentgenograms of this lesion show streaks of increased density radiating out

Fig 245 Solitary pulmonary metastasis from mammary carcinoma as seen roentgenographically

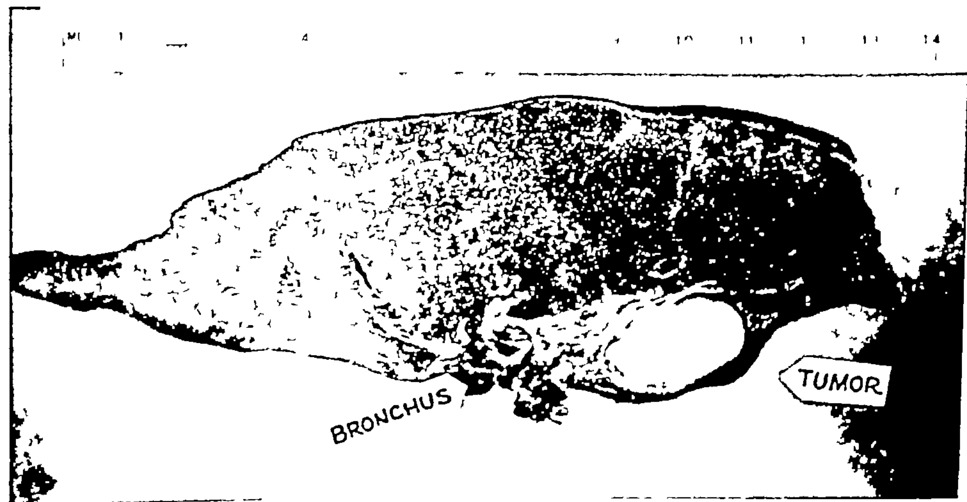


Fig 246 The gross appearance of the solitary pulmonary metastasis in the resected lung

not walk or lie down and slept sitting up near a window Edema of her legs had developed ten days before admission Circulatory supportive treatment was given Thoracentesis yielded 300 cc of grossly bloody fluid from the left pleura Nevertheless, her dyspnea and cyanosis increased and she died five days after admission to the hospital

At autopsy the lungs showed marked congestion and edema but only small gross foci of metastatic carcinoma There were metastases in many other organs Microscopically there was extensive carcinomatous permeation of the lung lymphatics The small pulmonary arteries contained tumor thrombi and showed marked fibrosis There was also non-suppurative lobular pneumonia

Good descriptions of the lymphangitic type of pulmonary metastasis have been written by Wu by Mueller and Sniffen and by Hauser and Steer



Fig 248 Dilated pulmonary lymphatics filled with carcinoma cells in the lymphangitic type of metastasis from mammary carcinoma.

Some of the previous writers on the subject have assumed that the permeation of pulmonary lymphatics which is such a striking feature of this type of metastasis occurs in a centrifugal direction from the hilar nodes out into the lung fields, and that the metastases first reach the hilar nodes from the primary lesion via lymphatic routes This assumption does not fit into our knowledge of the routes of spread of breast carcinoma The posterior mediastinal peritracheobronchial and intrapulmonary lymph nodes that drain the lungs have no direct lymphatic connection with the breast, and it is unlikely that lymphatic metastases from breast carcinoma go directly to them It is more reasonable to think that the disease reaches the lungs via the usual venous route The tumor thrombi in

from the hilum diffusely into the lung fields Both lungs are usually involved Figure 247 illustrates the roentgenographic appearance of this type of metastasis

At autopsy the findings do not show the massive involvement by carcinoma commonly seen with the nodular type of metastasis The lungs are firm and edematous Microscopical study shows the peribronchial and perivascular lymphatics to be filled with carcinoma cells The small arteries and arterioles

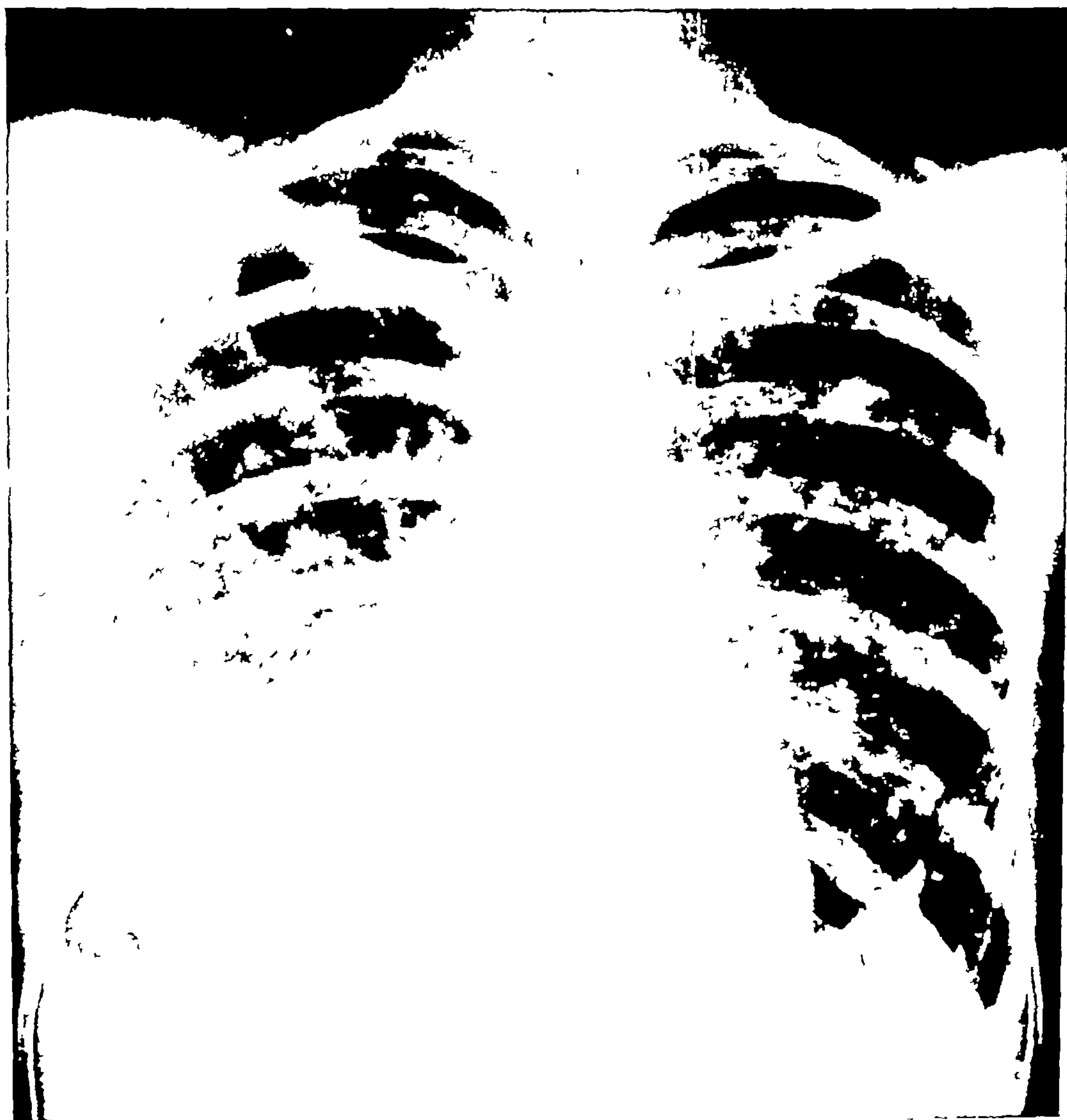


Fig 247 The roentgenographic appearance of the lymphangitic type of pulmonary metastasis from mammary carcinoma

contain tumor thrombi and show a remarkable degree of fibrosis It is these lymphatics distended with carcinoma and these fibrosed arteries that produce the linear x-ray shadows radiating from the hilum Figure 248 shows the dilated lymphatics filled with carcinoma cells in the lungs of one of our patients with the lymphangitic type of metastasis A summary of her case history follows

R. B , was admitted to the Delafield Hospital in acute respiratory distress She had had a left mastectomy in another hospital three years previously for carcinoma Six weeks before admission she developed dyspnea This rapidly increased until she could

not walk or lie down and slept sitting up near a window Edema of her legs had developed ten days before admission Circulatory supportive treatment was given Thoracentesis yielded 300 cc. of grossly bloody fluid from the left pleura Nevertheless, her dyspnea and cyanosis increased and she died five days after admission to the hospital

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the pulmonary arteries are evidence of this fact The peculiar feature of the lymphangitic type of metastasis is that an unusual fibrotic reaction to the presence of the carcinoma develops, and the fibrosis blocks lymph and blood vessels and permits the carcinoma to permeate the lymphatics in the normal centripetal direction of lymphatic drainage toward the hilar nodes, as well as peripherally toward the pleura

Pleural Metastasis

Pleural involvement develops sooner or later in the great majority of patients with breast carcinoma metastases in the lungs Abrams found pleural involvement at autopsy in 83 7 per cent of the cases with lung metastases In some of these patients pleurisy, evidenced by pleuritic pain and pleural effusion, is the first sign that the disease has reached the lungs There may be no roentgeno-

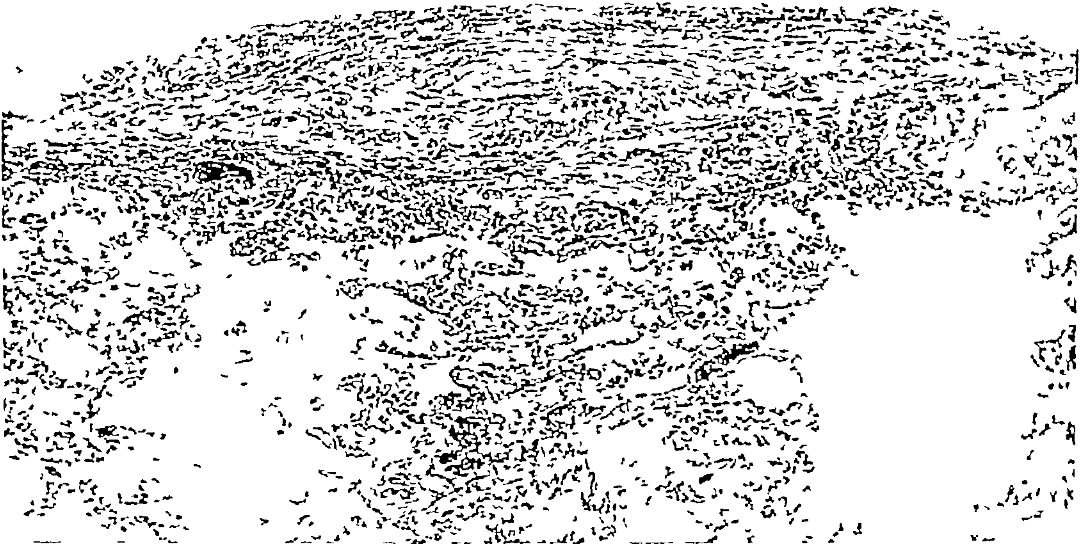


Fig 249 The microscopic appearance of a pleural focus of metastatic mammary carcinoma

graphic evidence of the pulmonary parenchymal involvement at this stage It may be assumed to exist, however, because the usual route of carcinoma to the pleura is from blood-borne emboli in the pulmonary arteries which grow and infiltrate the lung From these parenchymal foci the disease permeates the superficial lymphatic network of the lung and reaches the pleura Nodules of carcinoma beneath the visceral pleura break through it, permitting carcinoma cells to escape into the pleural cavity and producing pleural effusion In about 10 per cent of the cases the fluid is grossly bloody Carcinoma cells can often be identified in this fluid when it is centrifuged and the cell block thus obtained studied microscopically Luse and Reagan, in a special study of the cells of malignant tumors in effusions, were able to identify carcinoma cells in 66 6 per cent of their specimens of pleural fluid from patients with breast carcinoma

The free floating carcinoma cells in the pleural effusion can presumably implant upon the surface of the pleura and grow, because nodules are much more

frequently seen in the dorsal and basal portions of the pleural cavity where gravity would favor implantation

Figure 249 shows a microscopic focus of breast carcinoma on the surface of the pleura probably resulting from an implant

It is of course possible for breast carcinoma that infiltrates the thoracic wall to penetrate through it and get into the pleural cavity by way of the parietal pleura This is certainly an unlikely route in patients in whom effective treatment has eradicated the local primary disease and no recurrence has developed on the chest wall

In some patients the amount of pleural effusion is small and the degree of fibrous thickening of the pleura great In other patients the amount of serum that accumulates in the pleural cavities is very great Two or three thousand cc may be accumulated every day or so Patients cannot tolerate this condition for long

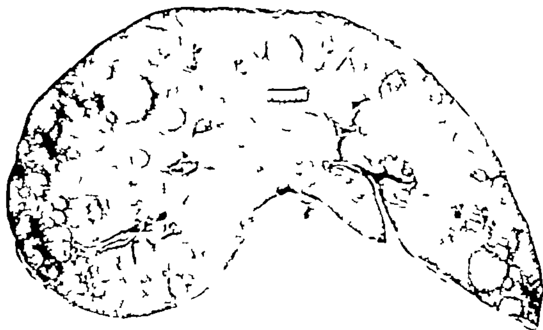


Fig 250 The gross appearance of metastatic mammary carcinoma in the liver

Liver Metastases

The liver competes closely with the lungs as a frequent site of metastases from breast carcinoma When metastases escaping from the lungs through the pulmonary veins get into the systemic arterial circulation they reach the liver through the hepatic artery They grow to form spherical masses scattered throughout the liver substance Figure 250 shows their usual appearance Liver metastases usually produce few if any symptoms until an advanced stage is reached when the liver may become so large as to cause abdominal distress The obstructive jaundice that sometimes develops may be accompanied by pruritus

Metastasis to Bones

Metastasis of breast carcinoma to bones is probably as frequent as if not more frequent, than metastases to lungs and liver Since no pathologist has systemati

the pulmonary arteries are evidence of this fact The peculiar feature of the lymphangitic type of metastasis is that an unusual fibrotic reaction to the presence of the carcinoma develops, and the fibrosis blocks lymph and blood vessels and permits the carcinoma to permeate the lymphatics in the normal centripetal direction of lymphatic drainage toward the hilar nodes, as well as peripherally toward the pleura

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in the bone we at the Delafield have been taught by Sproul to distinguish four types of metastases My illustrations for these four types are photographs of actual sections cut from vertebrae and decalcified and stained in the usual way

1 The *intertrabecular type* (Fig 251) Here the bone trabeculae which are shown in black are almost intact but the marrow spaces between the trabeculae



Fig. 251 The intertrabecular type of mammary carcinoma metastasis to a vertebra

are filled with carcinoma. It is understandable why this type of metastasis cannot be detected roentgenologically We subscribe fully to Schinz s statement that "The great majority of skeletal metastases merely cause a displacement of the bone marrow and do not produce any structural changes in the calcified bony tissue. They are not roentgenologically demonstrable

2. The *osteolytic type* (Fig 252) The bone trabeculae are to a large extent destroyed by the carcinoma This change in its early stage may have the roent

cally investigated the frequency of metastasis in all of the bones in which metastases are likely to be found, we do not really know what the true incidence of bone involvement is At the most pathologists have at autopsy taken sections at random from several of the vertebrae, and sometimes from ribs or pelvic bones Kitain, and Turner and Jaffe, reported bone involvement in some 56 per cent of cases This figure is certainly too low Abrams is nearer the truth with his figure of 77 per cent

Unfortunately, roentgenograms do not give us as accurate information on this question as autopsy studies Even when the entire skeleton is systematically studied a high percentage of bone metastases are not visualized Twenty-five years ago Chasin showed that in the vertebrae defects of from 1 to 1 5 cm diameter, produced by experimentally removing portions of the spongiosa, could not be demonstrated by the usual anteroposterior roentgenograms These findings were confirmed by Bohmig and Prevôt Recently, Bachman and Sproul, at the Delafield Hospital, have carried out a similar but more precise study, correlating radiographic and autopsy findings In a series of 59 autopsies Sproul found metastases in the vertebrae of 31 Bachman studied the vertebrae radiographically in these patients during the terminal stage of their disease, using the most elaborate techniques, including laminograms At autopsy the vertebrae were dissected out and Bachman made roentgenograms of them Nevertheless he was able to demonstrate metastases radiographically in only 15 of the 31 cases in which the microscope proved their presence These findings are shown in Table 68

Table 68 Correlation of Radiographic and Autopsy Findings
(Bachman and Sproul, Delafield Hospital)

Number of cases	Pathological findings	Radiographic findings			
		Correct x-ray diagnosis	Metastasis not visualized	False positive	Total
28	No vertebral metastasis at autopsy	27	—	1	28
31	Vertebral metastasis at autopsy				
	osteoplastic	8	11	0	19
	osteolytic	4	1	0	5
	mixed	2	0	0	2
	intertrabecular	1	4	0	5
		15	16	1	31
59	Total cases	42	16	1	59

As Bachman and Sproul's table shows, the degree of success with which roentgenograms reveal metastases in bone depends to a considerable extent upon the manner in which the disease grows in the bone Roentgenologists have been accustomed to classify bone metastases from breast carcinoma as osteolytic or osteoplastic This is too simple a classification In terms of the actual pathology

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2. The *osteolytic type* (Fig 252) The bone trabeculae are to a large extent destroyed by the carcinoma This change in its early stage, may have the roent

genological appearance of bone atrophy, but eventually its metastatic character is betrayed by the irregular defects that develop in the bone In the vertebrae the pedicles, the spinous process, or the body, including part of the cortex, may be destroyed The involved vertebrae are usually compressed and collapsed as the



Fig 252 The osteolytic type of mammary carcinoma metastasis to a vertebra

disease progresses Figure 253 shows compression of the sixth and seventh dorsal vertebrae due to metastases The roentgenological appearance of osteolytic metastasis in the pelvic bones and the upper end of the femur, and in the skull, is shown in Figures 254 and 255 The bones are seen to be riddled with irregular

moth-eaten defects The osteolytic type is overwhelmingly the most frequent of the types of bone metastasis of breast carcinoma that can be visualized roentgenologically

3 The *osteoplastic type* (Fig 256) The trabeculae are thickened They coalesce to form irregular osseous masses The bones assume an abnormally dense mottled or marbled appearance Periosteal thickening may lead to an actual increase in the volume of the bone Figures 257 and 258 show the roentgenographic appear



Fig 253 Compression of the 6th and 7th dorsal vertebrae due to osteolytic metastasis from mammary carcinoma as seen roentgenographically

ance of the osteoplastic type of metastasis from breast carcinoma in the skull and in the pelvic bones and the upper end of the femur Not more than 5 to 10 per cent of bone metastases from breast carcinoma are of the osteoplastic type

4 The *mixed type* A fourth type of bone metastases might be called the mixed type (Fig 259) in which the features of the other types are intermingled.

Metastases reach the bones through the blood stream. There are two routes One is from metastases in the lungs that break through the pulmonary capillary network and are carried back to the left heart which pumps them through the arterial circulation to reach the bones A second route to the bones one that has

not been recognized until recently, is through the vertebral system of veins As I described in Chapter 1, the vertebral veins provide a route via the intercostal veins of the chest wall, directly to the spine, the pelvic bones, and the skull, a route that is entirely separate from the caval route through the lungs and the systemic arterial circulation

We have no way of knowing which of these two routes is the predominant one for carcinoma emboli reaching the bones Although the most frequent sites of metastases are in the bones with vertebral vein connections, these same bones,



Fig 254 The roentgenographic appearance of osteolytic metastasis from mammary carcinoma to the pelvic bones and femur

particularly the lower vertebrae, are the ones containing the most red marrow Carcinoma emboli seem to find their most favorable environment for growth in the large and relatively quiet lakes of blood in the marrow of the lower vertebrae

Proof that carcinoma reaches the bones through the vertebral vein system is provided by cases in which bone metastasis occurs without lung involvement The following case is such a one

Mrs E P , a housewife aged 39, consulted me on July 6, 1941, for a tumor of her right breast that she had discovered five days previously

Examination revealed a 3 x 2 cm firm tumor in the inner lower sector of the right breast, just beyond the areolar edge There was retraction of the skin over the lesion In the right axilla there was a single 1 cm firm movable node

At operation frozen section showed the lesion to be a carcinoma Radical mastectomy with Thiersch graft was carried out Pathological study of the specimen showed a mod erately undifferentiated carcinoma Twenty three lymph nodes were dissected from the specimen. Three of these two from the lower axilla and one from the apex of the axilla contained metastasis

She was well until September 1944 when she began to have pain in the cervical region suggesting metastasis X ray films at this time showed nothing more than osteo-

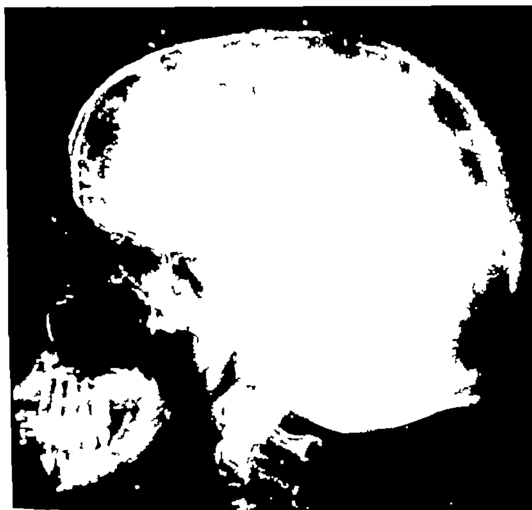


Fig. 255 The roentgenographic appearance of osteolytic metastasis from mammary carcinoma to the skull

arthritis of the cervical spine in the opinion of the roentgenologists. The pain in the cervical region persisted, although not severe In March 1945 she complained of pain in the left lateral chest region Films at this time showed metastases in the seventh and ninth left ribs, as well as in the cervical spine Radiotherapy to the cervical region and the left costal area gave her good palliative relief

In May 1945 she developed pain in the left elbow region, and films showed destruc tion of the medial condyle of the left humerus This area was irradiated with relief of pain, and reduction in the size of the lesion in the bone.

She was comparatively well until February 1947 when she began to have pain in the lower back. X-rays showed metastasis in T6 She was admitted to the hospital again and the thoracic spine irradiated. This course of radiation relieved her somewhat, but not

completely She was therefore put for the first time upon testosterone, intramuscularly

She had a relatively good summer during 1947 but was annoyed by the hoarseness and hirsutism which developed from the androgen By October, 1947, however, the pain in her back and pelvis had increased Films at this time showed progression of the metastases in the thoracic spine, T3, T6, T7, and T12 being involved The fifth lumbar vertebra and the right ilium now showed involvement She was admitted to the hospital again on October 30, 1947, and the lower spine and pelvis were irradiated with fairly good symptomatic relief She continued to take testosterone

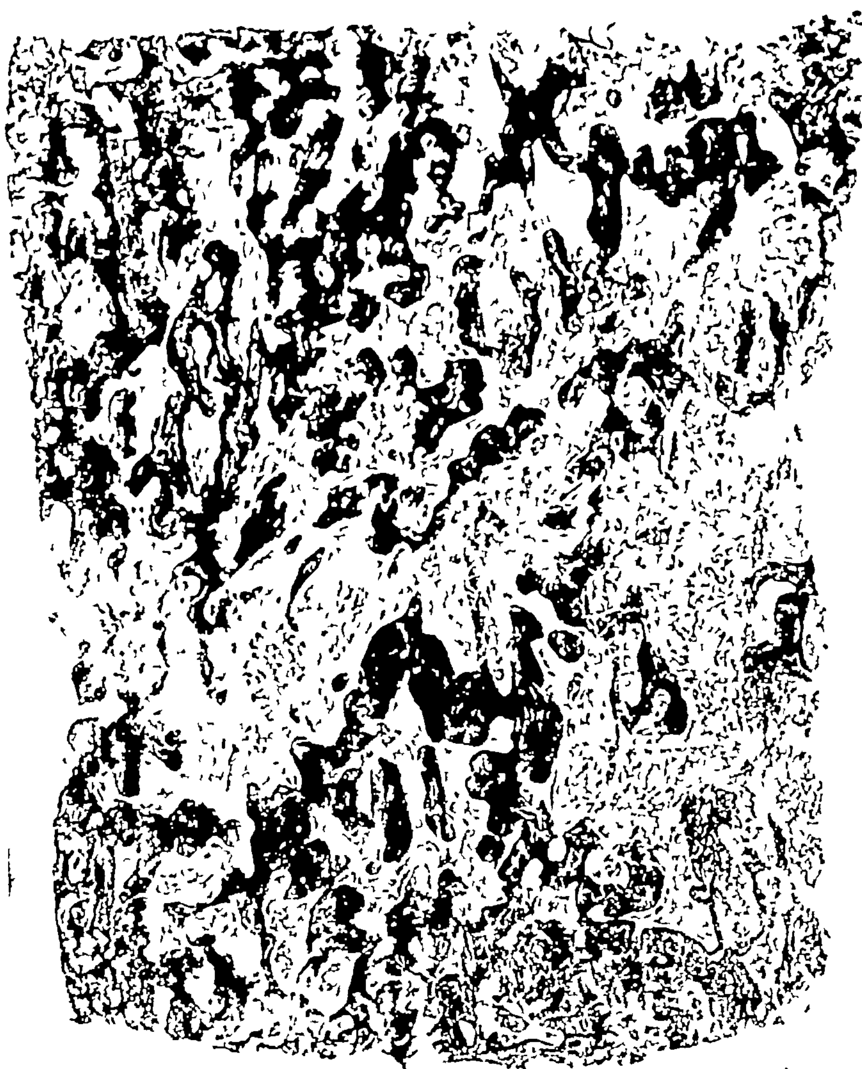


Fig 256 The osteoplastic type of mammary carcinoma metastasis to a vertebra

In May, 1947, a small new carcinoma was discovered in the upper outer sector of the left breast Since it did not seem wise to attempt to treat it at all locally, in view of her widespread metastases nothing was done for it By May, 1948, it had reached 4 cm in diameter By January, 1949, it was 5 cm in diameter During this period she had taken androgen consistently, yet the hormone had no apparent effect upon the progress of this new carcinoma

During 1948, she continued to get along fairly well, although her x-rays showed progressive destruction of the pelvic bones and lumbar vertebrae These bones were treated by irradiation with considerable relief Films showed some filling in of a particularly large area of destruction in the right iliac bone She continued to take androgen, although not regularly, and by mouth rather than intramuscularly She objected

strongly to the secondary changes which the androgen produced although the fact that she looked and felt amazingly well most of the time was without doubt to a considerable extent due to the hormone treatment After July 1948 she refused to take more hormone because of its unpleasant side effects

In the early months of 1949 her back and legs were giving her almost no trouble She was able to drive her car and be up and about most of the time Her cervical spine and ribs now began to trouble her increasingly The cervical vertebrae particularly C4 and C5 showed a great degree of destruction and she began to have forward dislocation of these vertebrae She was given further radiation to the cervical spine again with a fair degree of relief

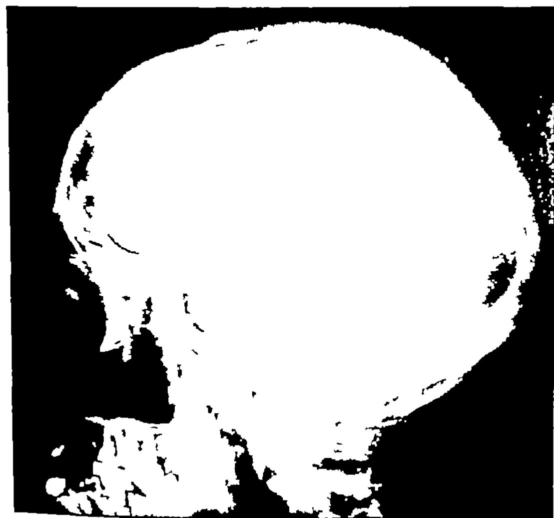


Fig 257 The roentgenographic appearance of osteoplastic metastasis from mammary carcinoma to the skull

During the latter part of 1949 however her neck pain became more and more troublesome. In October she was again admitted to the hospital and the cervical spine was again irradiated An area of extensive destruction in the upper right femur was also treated at this time She had fair relief from her leg and neck pain

In the spring of 1950 she began to have so much pain on motion that she began to spend most of her time in bed and from this time onward she was bed ridden. She was admitted to the hospital in April 1950 for further radiation of her thoracic spine. At this time it was necessary to do a palliative local excision of her left breast carcinoma. This contralateral breast carcinoma had slowly grown since its detection in May 1947 until it reached 6 cm in diameter The skin over it was reddened and ulceration seemed imminent.

In the fall of 1950, she began to require morphine for the first time, but even with this, she was not comfortable It was therefore decided in January, 1951, to do a unilateral lobotomy This was performed by Dr T Scarff and gave her good relief of pain until February 6, when she had a spontaneous fracture of her right femur From this point on she required increasingly heavy sedation until her death on February 22, 1951, nine years and four months after radical mastectomy.

At autopsy widespread bone metastases, as well as nodular metastases in the liver, were found The lungs, however, were entirely free of carcinoma, both grossly and



Fig 258 The roentgenographic appearance of osteoplastic metastasis from mammary carcinoma to the pelvic bones and femur

microscopically It is difficult to escape the conclusion that this patient's carcinoma reached her vertebrae, which were the first bones involved, through the vertebral system of veins If the disease had reached the vertebrae through the caval route and the lungs, it should have been found in the lungs at death more than nine years later

A generation ago Sampson Handley, in advancing his theory of the spread of carcinoma by lymphatic permeation, explained bone metastasis as the result of a process of continuous permeation of the lymphatics in fascial planes. Some students of the question, like Carnett and Howell, were convinced of the correctness

of Handley's explanation but most pathologists have opposed it Piney in an important study presented in 1922 was unable to demonstrate any lymphatics in bone marrow and he concluded that metastases to the bone marrow must be

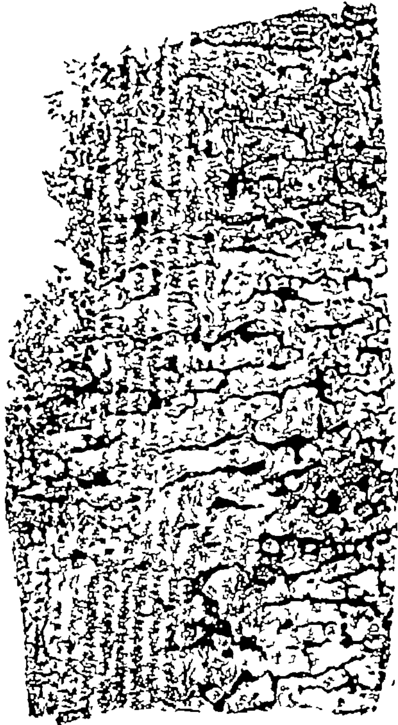


Fig. 259 The mixed type of mammary carcinoma metastasis to a vertebra.

blood borne He explained the relative freedom of the distal bones of the limbs from carcinoma metastases as due to the absence of red marrow in these bones The red marrow according to Piney is the place in which the bed of the blood stream widens, the course of the vessels becomes more complicated, and the conditions for the lodgment of emboli become correspondingly more favorable.

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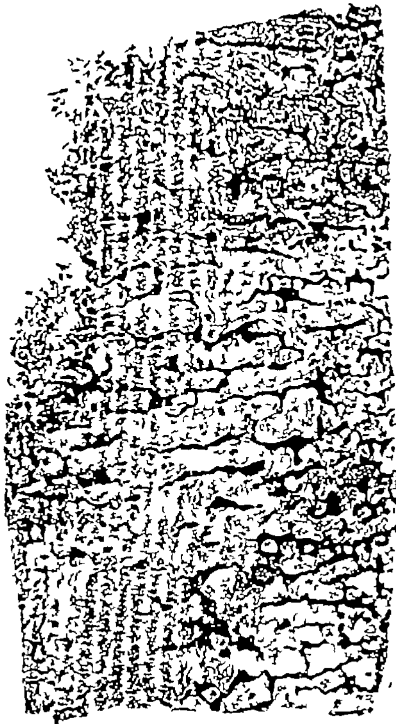


Fig 259 The mixed type of mammary carcinoma metastasis to a vertebra

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The blood stream slows in the red marrow, and its solid elements, such as tumor emboli, settle at the periphery of the vascular bed and proliferate there

According to Handley's theory, the lymph nodes and fasciae in the region of distant bone metastases are assumed to have been involved by the permeation process before the disease reaches the bones To test the validity of this theory, Willis made special studies of the lymph nodes and fascia regional to skeletal metastases In 11 cases with metastases to the femur, he found the inguinal lymph nodes to be involved in only one case Moreover, thorough microscopic examination of the deep fascia from several parts of the thigh and buttock, and of the periosteum stripped from the bone near the metastases showed no evidence of cancer cells

Handley wrote that "The liability of a bone to cancer metastases increases with its proximity to the site of the primary growth " Modern x-ray and autopsy evidence have shown that this is not true in cancer of the breast The sternum and ribs are not affected earlier and more frequently than other bones as Handley's theory would imply The most extensive roentgenological data on this point come from the Mayo Clinic where Sutherland and his associates studied the distribution of the lesions as shown by x-ray in a series of 628 cases of skeletal metastasis from breast carcinoma The distribution of the metastases was as follows

	%
Pelvis	33 9
Lumbar spine	20 7
Ribs	13 5
Femur	11 8
Shoulder girdle	5 3
Skull	4 9
Thoracic spine	4 6
Humerus	2 8
Cervical spine	1 3
Lower extremity	0 1
Upper extremity	0 8

More accurate information as to which bones are most often involved by metastases in breast carcinoma has been derived from studies that utilize both roentgenological and autopsy evidence, such as that by Lenz and Freid Their data (Table 69) included 81 cases of breast carcinoma in which the existence of bone metastases had been proved roentgenologically or by autopsy The predilection of the lower vertebrae and the pelvic bones to develop metastases is apparent from these data

The smaller and the more peripheral the bones of the extremities, the less likely they are to be involved by metastases Only in rare cases in which the entire skeleton is riddled with metastases, as in that described by Bendick and Jacobs, is involvement of the metacarpal bones and phalanges seen

Fracture of the femurs or humeri, and sometimes of the ribs or clavicle, weakened by metastases, are not infrequent In Lenz and Freid's series there were fractures of one or more bones in 26 per cent of the cases In our own experience

the incidence of fractures has not been as high and is closer to Copeland's figure of 15 per cent

Even though most of the bone has been replaced by carcinoma at the site of one of these pathological fractures the normal healing reaction as expressed by

Table 69 Carcinoma of the Breast Anatomical Distribution in 81 Cases of Skeletal Metastases (Lenz and Freid 1931)

General localization	Per cent	Specific localization	Per cent	Homolateral Heterolateral Bilateral	
Pelvis	62	Ischium	37		
		Ilium	58		
		Pubis	56		
Spine	59	Cervical	13		
		Dorsal	40		
		Lumbar	57		
		Sacral	38		
Femur	54			Bilateral	31
				Heterolateral	8
				Homolateral	5
Ribs	39			Bilateral	20
				Heterolateral	5
				Homolateral	7
Skull	35				
Humerus	27			Bilateral	11
				Heterolateral	5
				Homolateral	6
Scapula	16			Bilateral	8
				Heterolateral	4
				Homolateral	1
Clavicle	14			Homolateral	1
				Bilateral	5
				Heterolateral	6
Tibia	3			Homolateral	2
				Heterolateral	1
Sternum	1				
Radius	1				
Ulna	1				
Hands	1				
Fibula	1				
Bones of feet	1				

callus formation is often sufficient to achieve bony union if the fragments are adequately fixed. Figure 260*a* shows a pathological fracture through a large metastasis in the humerus from a breast carcinoma. It was immobilized and irradiated, and good union resulted Figure 260*b* shows its appearance a year later

The blood stream slows in the red marrow, and its solid elements, such as tumor emboli, settle at the periphery of the vascular bed and proliferate there.

According to Handley's theory, the lymph nodes and fasciae in the region of distant bone metastases are assumed to have been involved by the permeation process before the disease reaches the bones. To test the validity of this theory, Willis made special studies of the lymph nodes and fascia regional to skeletal metastases. In 11 cases with metastases to the femur, he found the inguinal lymph nodes to be involved in only one case. Moreover, thorough microscopic examination of the deep fascia from several parts of the thigh and buttock, and of the periosteum stripped from the bone near the metastases showed no evidence of cancer cells.

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	%
Pelvis	33.9
Lumbar spine	20.7
Ribs	13.5
Femur	11.8
Shoulder girdle	5.3
Skull	4.9
Thoracic spine	4.6
Humerus	2.8
Cervical spine	1.3
Lower extremity	0.1
Upper extremity	0.8

More accurate information as to which bones are most often involved by metastases in breast carcinoma has been derived from studies that utilize both roentgenological and autopsy evidence, such as that by Lenz and Freid. Their data (Table 69) included 81 cases of breast carcinoma in which the existence of bone metastases had been proved roentgenologically or by autopsy. The predilection of the lower vertebrae and the pelvic bones to develop metastases is apparent from these data.

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Fracture of the femurs or humeri, and sometimes of the ribs or clavicle, weakened by metastases, are not infrequent. In Lenz and Freid's series there were fractures of one or more bones in 26 per cent of the cases. In our own experience

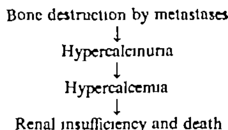
roentgenological evidence of the lesion by some months. Lenz and Freid described 7 cases in which the pain preceded the roentgenological visualization of the bone lesion by from six to twelve months. I have seen many patients with this sequence and I have learned that it is wisest to assume that bone metastases have developed, even though x ray studies reveal nothing abnormal, in patients with breast carcinoma who develop back or leg pain, or pain over other bones, for which no other good explanation is apparent.

There are certain features of the early stage of pain produced by bone metastases that suggest the diagnosis. Pain is at first apt to be noted when the patient is jarred or jolted, as when she misses her step in walking, or coughs or sneezes. The pain is not constant. It develops when the patient gets up out of bed or from a chair, and it is aggravated by motion. When she lies or sits quietly it disappears.

There are, of course, some patients whose bone metastases produce no pain at all. I have seen several whose skeleton was riddled with metastases, yet they did not complain of pain. I know of no adequate explanation for this paradox.

When breast carcinoma destroys bone important changes in mineral and protein metabolism occur. Laszlo and his associates at the Montefiore Hospital have carried out pioneer investigations in this field. As a result of their work we are beginning to have some understanding of the complex metabolism of these patients. Marked osteolysis is characterized by excessive urinary calcium excretion, inversion of the urine-to-fecal calcium ratio, negative calcium and phosphorus balance, and hyperphosphaturia. When the degree of osteolysis becomes excessive hypercalcemia occurs. The disease progresses in waves of osteolysis and attempt at repair. Renal impairment finally results from the prolonged hypercalcinuria and hypercalcemia.

This sequence of events may be indicated diagrammatically as follows:



Laszlo has written the best description of the clinical syndrome of hypercalcemia. It occurred in 14 per cent of a series of patients with bone metastases that he studied. The syndrome included a characteristic triad of symptoms consisting of gastrointestinal disturbances (nausea, vomiting, and constipation), mental changes (lassitude, lethargy, stupor and coma), and renal impairment (oliguria, nitrogen retention). The hypercalcemic syndrome occurs spontaneously in patients with osteolytic metastasis. It can also be induced by the administration of androgen or estrogen (Laszlo et al., Herrmann et al.). The therapy of patients with hypercalcemia consists chiefly of forcing fluids by the oral and intravenous routes. The drop in urinary calcium marks the point at which symptoms are relieved.

In the osteoplastic type of bone metastases calcium retention instead of calcium loss occurs. There is a subnormal urinary calcium excretion.

Hummel described the pathological aspects of this healing process in several cases

It is therefore important to try to obtain healing of pathological fractures Suitable orthopedic methods for fixing the fragments should be used, and in addition radiotherapy should be given to the lesion to hold the carcinoma in check

Pain and, less frequently, tenderness on pressure or percussion, are the clinical signs of bone metastases The pain is often referred along the course of the nerves



a b

Fig 260 The roentgenographic appearance of metastasis from mammary carcinoma to the humerus *a*, pathological fracture through the metastasis, *b*, immobilization and irradiation with good union one year later

that come into contact with the lesion Thus metastases in lumbar or sacral vertebrae contiguous to the dorsal roots of the lumbar or sacral plexuses produce pain that radiates into the thigh and leg, usually on one side Tenderness on pressure is often present over metastases in ribs Local pain and tenderness are presumably due either to pressure on the periosteum or to actual infiltration of the nerves in the periosteum, since bone itself does not contain sensory nerves

An important feature of the natural history of bone metastases is that pain is usually the first indication of the presence of the bone lesion, and often precedes

have a predilection for the posterior portion of the uvea They produce failing vision with eventual retinal detachment Both eyes are often involved Good case reports are found in papers by Jensen Bedell Boemke and Merriam

Less Frequent Forms of Metastasis

Carcinoma of the breast may metastasize to any part of the body and there are many reports of unusual and bizarre metastases Some of these follow *Tongue* (Fink and Garb) *Mandible* (Sonntag Lüdin Burket Adair and Herrmann) *Parotid* (Herrmann and Adair) *Gasserian ganglion* (Fitzwilliams and Fell) *Hypophysis* (Cain) *Placenta* (Cross et al) *Vagina* (Held) *Umbilicus* (Falkinburg and Savran)

The Natural Duration of Carcinoma of the Breast

An accurate concept of the natural duration of untreated carcinoma of the breast is essential to our understanding of variations in the course of the disease as well as to our correct assessment of the value of different forms of treatment

The distinguished English statistician Major Greenwood was the first to study the question adequately In 1926 he analyzed data from hospitals in London Glasgow and Manchester regarding the length of life from the first symptom to death in 651 patients with breast carcinoma who received no treatment The mean duration of life in these patients was 38 3 months

Daland studied the course of breast carcinoma in 100 patients from two Boston Hospitals to whom no surgical or radiation treatment had been given The mean duration of life from the first symptom to death was 39 5 months

Nathanson and Welch also reported the duration of life from onset to death in a series of 100 cases of breast carcinoma Their series included 50 of the cases that had been reported previously by Daland, and their findings agreed very closely with Daland s.

Wade tabulated the duration of life from onset to death in a series of 26 cases from Leeds The mean duration was 32 6 months

Now that the palliative value of hormonal treatment of breast carcinoma has been discovered and almost all patients are likely to be treated by this easy method, it is unlikely that more data concerning the duration of life in patients who have received no treatment at all will be available. It is therefore important that we draw what conclusions we can from the approximate 800 cases of untreated breast carcinoma reported in these several studies We can conclude, first of all, that spontaneous cure of breast carcinoma has not been observed Spontaneous cure is a favorite theory of arm-chair students of the disease Those of us who work with breast carcinoma do not see it

We may also conclude that there is great variation in the natural duration of the disease The mean duration of disease from onset of symptoms to death in 777 cases (after Wade) was 38 5 months. Yet in some patients with unusually malignant disease death resulted in as short a time as three months In occasional patients the natural course of the disease was very long indeed. In Greenwood s data there were two women whose disease lasted thirty years Daland referred to one patient who was still alive at the age of 80 after having had breast carcinoma for 35 5 years Nathanson and Welch had one patient whose carcinoma lasted

Schilling and Laszlo have recently devised a calcium tolerance test that promises to be useful in determining the metabolic status of patients with bone metastases A test dose of calcium gluconate is given intravenously under controlled metabolic conditions and urinary and blood calcium levels studied at intervals These excretion rates reflect changes in the bones earlier and more accurately than roentgenographic studies

Griboff and his associates, also at the Montefiore Hospital, carried out a special study of the relationship between serum calcium and alkaline phosphatase values in patients with hypercalcemia due to bone metastases from breast carcinoma Their results suggested that the onset of hypercalcemia is preceded by a premonitory fall in serum alkaline phosphatase activity, but other investigators have not as yet confirmed this finding

Bodansky has recently reported studies of serum-phosphohexose-isomerase in patients with bone metastases that suggest that there is some correlation between the progress of the bone metastases and the increase in serum-isomerase activity

Metastasis to the Brain

When the brain is examined and metastases carefully sought for they will be found to be fairly frequent in cases of carcinoma of the breast Abrams found them in 29 per cent of his series of autopsies

Brain metastases are important because of the therapeutic problem they present They produce clinical signs of increased intracranial pressure such as headache and vomiting, disturbances of vision, and convulsive seizures, thus simulating primary brain tumors Neurological surgeons are well aware of this diagnostic problem They also know that breast carcinoma is a most frequent source of brain metastases, and they have learned to search for a primary breast lesion Grant reported 15 of a series of 49 cases of metastasis to the brain as due to breast carcinoma, and Dunlap published a series of 95 secondary brain tumors of which 28 were due to breast carcinoma

These brain metastases may be situated in any part of the brain and they are usually multiple This latter fact, and the presence of metastases elsewhere, usually makes craniotomy impractical Rarely, brain metastases are solitary and cystic, as in the remarkable case described by Willis

Ovarian Metastasis

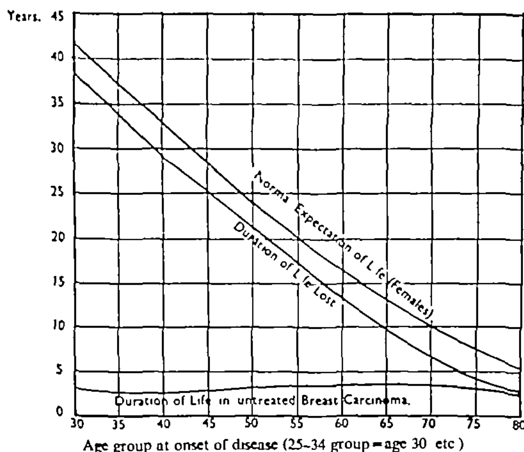
Metastasis to the ovaries is of special interest because of its implications in terms of hormonal metabolism The highest reported incidence is 23 per cent in Abrams' autopsy series Metastases have been found in a surprisingly high percentage of ovaries removed by surgeons for hormonal control of breast cancer Sicard found ovarian metastases in 11 of 38 such cases, Jáki and Korpássy found them in 6 of 15 cases and Dargent et al found them in 3 of 7 cases Even though the ovaries are grossly normal, they not infrequently prove to contain metastasis on careful microscopical study

Metastases to the Eye

Merriam states that of some 300 reported cases of metastatic tumor in the eye about 70 per cent have originated from carcinoma of the breast These metastases

Unfortunately these studies concerning the natural duration of the disease do not include information concerning microscopical grade

A second factor to be considered is the influence of the age of the patient upon the course of her carcinoma Since this question involves consideration of the normal expectation of life for females of different age groups it requires statistical treatment Wade s graph (Chart 18) shows the curves she plotted from her



Age group at onset of disease (25–34 group = age 30 etc)

Chart 18 Duration of life lost by patients with untreated breast carcinoma (756 cases) (after Wade)

calculations and indicates that the natural duration of untreated breast carcinoma is similar in all age groups, except for a slight increase in duration in the middle groups A wider variation in the natural duration is noted in the younger age groups

After all these statistical data have been considered I am nevertheless left with the clinical impression that carcinoma of the breast is more malignant when it occurs in the young than in the aged If this impression is correct, the contradiction which the statistical approach to the question provides is an example of the difficulty of measuring biological phenomena by statistical methods

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fifteen years One of Wade's patients lived twenty-two years after onset of symptoms and died at the age of 72

A patient of my own illustrates the exceedingly slow course that carcinoma of the breast may take

M S, a widowed laundry worker in the Presbyterian Hospital, aged 64, complained on 6/26/45 that she had a lump in her right breast She stated that she had had it for about seventeen years Examination showed a 2 cm hard tumor of the upper middle portion of her right breast The tumor was relatively movable beneath the skin and over the chest wall There were no retraction signs There was a 5 mm firm, movable node in the right axilla

The tumor was biopsied and proved to be a relatively undifferentiated carcinoma The patient had advanced hypertensive cardiovascular disease, and since her breast disease was not giving her any symptoms it was decided not to treat it

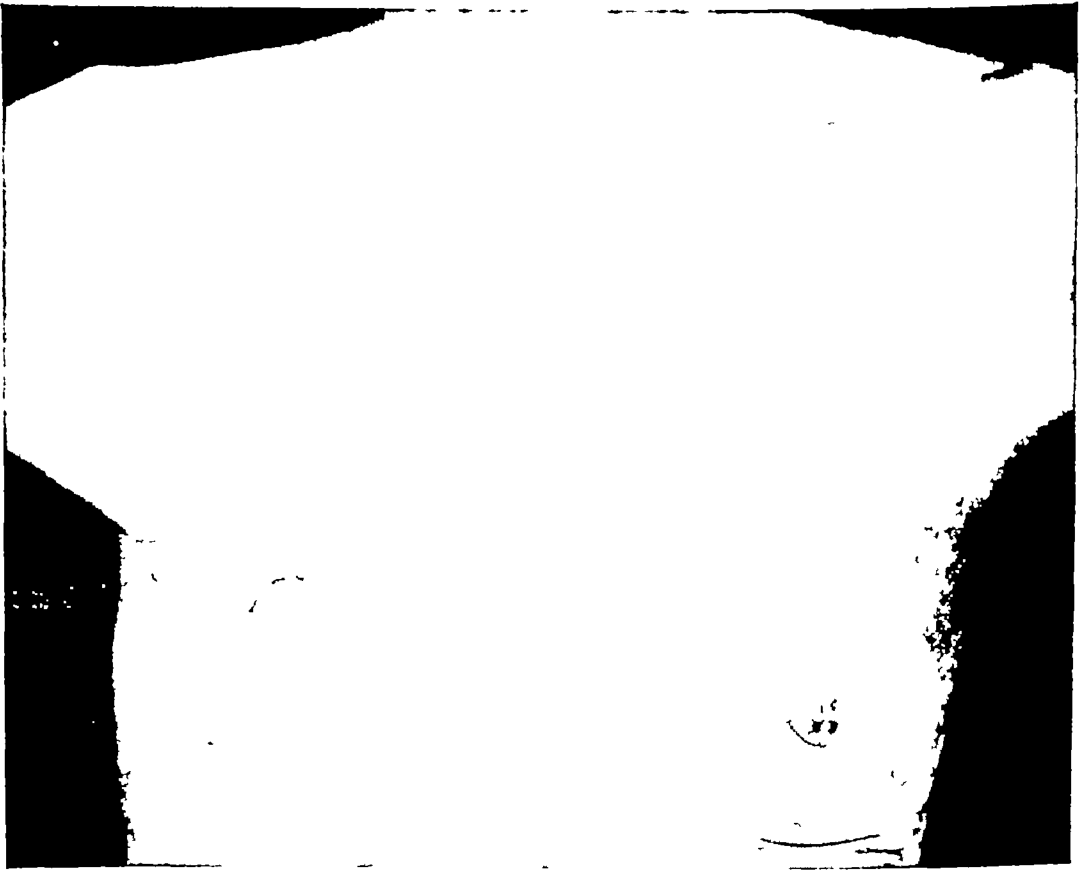


Fig 261 Carcinoma of the breast of 27 years' duration

The patient's carcinoma progressed exceedingly slowly When I last saw her in January, 1955, ten years after her tumor had been biopsied, and twenty-seven years after it had been discovered by the patient, it measured only 3 cm in diameter It had increased only 1 cm in diameter in ten years Retraction signs, including distortion of the areola and nipple had, however, developed (Fig 261) The axillary node measured about 8 mm in diameter

In seeking for an explanation of the great variation in the course of breast carcinoma two factors come to mind The first of these is the effect of the degree of differentiation, that is, the microscopical grade of malignancy of the tumor

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Table 71 Symptoms of Mammary Carcinoma

Symptom	Lane Claypon 508 cases	Truscott 787 cases	Harnett 2129 cases	Kaae 500 cases
A lump first no pain ever	39*	67.5	77.4	74
A lump first pain later	16.5	16		
Pain first	17.7*	10*	10*	12*/
Nipple discharge	7.4	7.5	2.2	2.7*
Nipple retraction	2*	3	2*	4.2*/
Nipple itching	1			
Nipple erosion				
Shrinkage of breast	2			
Ulcerated skin of breast		0.5		1.7*/
Found by M D	1	0.1	1.6	0.8*/

Table 72. Symptoms in 546 Personal Cases of Carcinoma of the Breast (1943–1954)

	Primary	Secondary	Total
Lump	369	51	420
Pain in breast	40	54	94
Tenderness on pressure over breast	3	5	8
Skin dimpling	21	7	28
Skin ulceration	0	2	2
Nipple retraction	14	9	23
Nipple discharge	13	8	21
Nipple erosion	9	2	11
Nipple itching	4	5	9
Breast enlarged	3	2	5
Breast shrunken	2	2	4
Generalized hardness of breast	1	1	2
Redness of skin	1	6	7
Skin nodules	0	1	1
Ecchymosis in skin	0	1	1
Axillary tumor	11	5	16
Arm pain	1	0	1
Arm swelling	1	0	1
Pain in back	2	0	2
Total	495	161	656
No symptoms. Disease discovered at physical examination	51		
Total	546		

CHAPTER 20

THE SYMPTOMS OF MAMMARY CARCINOMA

Women who develop mammary carcinoma usually discover their breast disease themselves Among our 1033 ward patients with the disease coming to the Presbyterian Hospital between 1915 and 1942, 91 6 per cent came complaining of breast symptoms In 5 9 per cent the disease was discovered by a physician during routine physical examination, the patient having been entirely unaware of her breast disease This fact is good evidence of the value of careful routine physical examination

The symptoms of which our patients who came to the Presbyterian Hospital between 1915 and 1942 complained are listed in Table 70 These data have been

Table 70 Symptoms in Primary Ward Cases of Breast Carcinoma
(Presbyterian Hospital 1915–1942)

Total number of primary ward cases	1033
Manner of diagnosis not stated	26, or 2 5%
Came to hospital complaining of symptoms elsewhere than in breast Breast carcinoma discovered during routine physical examination	61, or 5 9%
Came to hospital complaining of symptoms in breast	946, or 91 6%
Complained of tumor in breast	873, or 84 5%
Complained of other breast symptoms	73
Erosion of nipple	16
Pain in breast	27
Retraction of nipple	12
Enlargement of breast	14
Discharge from nipple	13
Itching of nipple	7
Redness of skin over breast	6
Generalized hardness of breast	5
Shrinkage of breast	1

compiled from the clinical histories taken by the intern staff No distinction is made between the primary or first symptoms that called the patient's attention to her breast disease, and secondary symptoms that developed subsequently

Similar data that have been presented by modern students of breast carcinoma are shown in Table 71

For a closer inquiry into the frequency and sequence of symptoms in carcinoma of the breast I have utilized the records of my own 546 private patients whom I saw between the years 1943 and 1954 I took these case histories personally The symptoms of which these patients complained are shown in Table 72

relied upon If a woman past the menopause at an age when the cyclical physiological pain due to breast engorgement is not to be expected experiences for the first time sharp pain localized in the breast the fact should of course suggest the possibility of carcinoma to her physician The physician s point of view regarding breast pain however is necessarily different from that of the layman In our propaganda to the public I believe that we would do well to emphasize the fact that a lump is the all important warning sign of breast cancer and that the lump is usually painless Much of my own time is spent reassuring patients who come to me with nothing more than breast pain of physiological origin

Retraction

Retraction signs were noted only infrequently by our patients In my personal series of 546 patients, only 28 noted skin dimpling while 4 noted shrinkage of the breast Twenty three noted retraction of the nipple These retraction signs were usually discovered while bathing or dressing A great many of my patients had perfectly obvious retraction signs and were entirely oblivious to them It is unlikely that we will be able to teach patients to inspect their own breasts critically enough to enable them to detect breast carcinoma by means of the retraction signs that it so often produces

Redness of the Skin

There were 7 patients who noted redness of the skin over the breast in my personal series of carcinomas In one of these in whom the entire breast was red edematous and indurated the disease was classified as the inflammatory type and as inoperable In a second patient also classified as inoperable there was redness and edema involving one third of the skin over the breast and in addition an axillary metastasis measuring 3 cm in transverse diameter

In 5 of the 7 patients with redness of the skin the carcinoma was classified as operable although comparatively advanced In 4 of the 5 there was also edema of the skin involving less than one third of the skin over the breast The redness was more extensive than the edema involving about one half of the skin over the breast In 2 of these 4 patients the redness was transitory disappearing with antibiotics and bed rest In the fifth patient the redness was not accompanied by edema.

None of the 5 patients was cured and I am inclined to regard redness of the skin of a sufficient degree to be noticed by the patient as a sign of far advanced disease even though the clinical picture is not that of the classical inflammatory type of carcinoma

Nipple Discharge

Spontaneous discharge from the nipple either watery serous, or bloody has been infrequent in our cases of carcinoma It occurred in only 1 4 per cent of the Presbyterian Hospital series of 946 cases of carcinoma In my personal series of 546 patients with carcinoma in which I personally took the history 21 or 3 8 per cent, had a spontaneous nipple discharge It was watery in one patient serous in 7 and bloody in 13

There are not many studies that report correctly *the frequency of nipple dis*

Tumor

From all these data it is obvious that the overwhelming majority of women with breast carcinoma become aware of their disease as a result of finding a breast lump The discovery is almost always accidental The patient s hand happens to encounter the tumor while she is bathing or dressing The tumor that a carcinoma produces in the breast is more easily felt by the patient than most other types of breast tumor because of its hardness The patient may not describe it as a lump but as merely an area of thickening The important point is that she usually recognizes that she feels something abnormal Patients occasionally find breast carcinomas as small as 5 mm in diameter This fact is striking evidence of the accuracy of their palpation

Pain

Pain, as a symptom of breast carcinoma, has recently been studied by River and by Corry. Both of these authors have stressed the frequency of local pain in the primary breast lesion River found it in 24 per cent of his patients, and Corry in 53 per cent The latter presented an elaborate classification of the type of pain encountered It was momentary and snatching (as if the breast had been suddenly pulled and then let go), or stabbing (single or multiple stabs), or continuous and aching (burning, gnawing, or dragging) The momentary and continuous types were about equally frequent.

My own experience with pain as a symptom of breast carcinoma has been rather different I have found pain to be an uncommon primary symptom In my personal series of 546 case histories it was the first symptom in only 40 patients, or 7.3 per cent It has also been an infrequent secondary symptom, occurring in only 10 per cent of my cases Pain, therefore, was a primary or secondary symptom in a total of only 17 3 per cent of my patients There were, in addition, 3 patients who complained of tenderness on pressure as a primary symptom, and 5 who mentioned tenderness as a secondary symptom

In taking the histories in my patients I have been careful not to emphasize or suggest pain as a symptom I ask the patient straight out what symptom called her attention to her breast. I then ask her (1) if she feels a lump, (2) if she has pain, and (3) if she has a nipple discharge or any other breast symptom I do not ask her first of all if she has pain and whether it is intermittent, continuous, or stabbing shooting, stinging, snatching, burning, gnawing, or aching I suspect that such leading questions suggest pain to these frightened and receptive patients The difference between Corry's data and my own can perhaps be explained by differences in the method of questioning

The one type of breast pain that is, in my experience, somewhat suggestive of carcinoma, is intermittent and sharp and is felt in the region of the tumor Patients have twinges of this kind of pain, usually occurring only infrequently, but of sufficient intensity to make them suspect breast disease Only 20 of the 94 patients who complained of pain in my personal series of 546 cases of breast carcinoma had this type of pain They described it as twinges of pain, or sharp, sticking, stinging shooting stabbing throbbing, or burning pain

I am led to conclude that pain is not a very important symptom of breast carcinoma Even in its most suggestive form it occurs too infrequently to be

relied upon If a woman past the menopause at an age when the cyclical physiological pain due to breast engorgement is not to be expected experiences for the first time sharp pain localized in the breast the fact should of course suggest the possibility of carcinoma to her physician The physician s point of view regarding breast pain however is necessarily different from that of the layman In our propaganda to the public I believe that we would do well to emphasize the fact that a lump is the all important warning sign of breast cancer and that the lump is usually painless Much of my own time is spent reassuring patients who come to me with nothing more than breast pain of physiological origin

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There are not many studies that report correctly *the frequency of nipple dis*

charge in carcinoma of the breast Patients with a discharge that is not spontaneous and has to be elicited by squeezing the breast, as well as patients with Paget's erosion of the nipple in which the eroded nipple surface oozes serum but there is no true discharge from the nipple ducts, should not be included I suspect that the comparatively high incidence of nipple discharge (7 5 per cent) that Truscott has reported can be explained by the inclusion of such cases Harnett comes nearer the truth with a 2 2 per cent incidence of nipple discharge in his series of 2,129 cases Hinchey reported that 3 2 per cent of his series of 742 patients with carcinoma had a nipple discharge In Wolpers' series of 414 cases of carcinoma 1 2 per cent had a bloody nipple discharge

There are more reports of the reverse relationship, namely, *the frequency of carcinoma in patients with nipple discharge* These reports can be divided into two groups, one with a high incidence of carcinoma and the other with a low incidence, depending upon the interpretation of the pathology of the papillary lesions As an example of the former, Judd, as well as Gray and Wood, from the Mayo Clinic, classified the lesions in 57 and 50 per cent, respectively, of their patients with a nipple discharge, as malignant Dr Stout and I believe that most of these "malignant" lesions were benign papillomas

In another series of 219 patients with nipple discharge from the University of Iowa, Donnelly reported that 44 per cent had carcinoma

Examples of reports with a lower frequency of carcinoma among patients with nipple discharge, based upon more critical pathological classification, are those from Johns Hopkins by Hart in 1927, and by Lewison and Chambers in 1951 In Hart's series of 77 patients with a nipple discharge, 10 4 per cent had malignant lesions In Lewison and Chambers' series of 114 patients with nipple discharge, 11 2 per cent had carcinoma Kilgore and his associates reported 14 cases of carcinoma among a total of 103 patients with a bloody nipple discharge

During the period 1943 to 1954 inclusive I studied a total of 118 private patients who came to me with a nipple discharge Twenty-one, or 18 per cent, proved to have carcinoma All but two of the patients with carcinoma had palpable tumors

It has been of great interest to Dr Stout and to me to correlate the presence and type of discharge with the pathological findings in the breast after its removal in these patients with carcinoma The cases fall into three groups, as shown in Table 73

These data lead me to the conclusion that discharge from the nipple occurs comparatively infrequently in breast carcinoma When it does occur it is usually due either to benign intraductal papilloma which happens to be coincident with carcinoma, or to the papillary type of carcinoma It is understandable that the papillary processes growing in the ducts in both of these lesions easily break off, and serum or blood escapes from the vessels in their stalks In a few cases we did not find an explanation for the nipple discharge, but we can conjecture that our microscopical sections missed the papillary lesions in these cases

Nipple Erosion

There were 11 patients in my personal series who noted erosion or crusting of the nipple due to the Paget's type of carcinoma Nine of the 11 had itching of the

Table 73. 21 Patients with Nipple Discharge among 546 Patients with Breast Carcinoma (Personal Series 1943–54)

Case	Type discharge	Duration discharge	Microscopical findings
A Patients with Coexistent Benign Intraductal Papilloma and Carcinoma			
L. W	Serous	45 years	Separate benign intraductal papilloma and undifferentiated carcinoma
R. N	Serous	12 months	Benign intraductal papilloma and adjacent moderately undifferentiated carcinoma
M B	Bloody	10 months	Multiple benign intraductal papilloma and (bilateral) intraductal carcinoma
H M	Bloody	2 months	Multiple benign intraductal papilloma and (bilateral) adenosis. Moderately undifferentiated carcinoma
B Patients with Papillary Carcinoma			
I W	Bloody	5 months	Partly intraductal papillary carcinoma Mostly moderately undifferentiated carcinoma
L. C.	Bloody	5 months	Intraductal papillary and en rognon" type carcinoma
D P	Bloody	9 months	Papillary intraductal carcinoma
H K	Serous	33 months	Intraductal papillary carcinoma
R. P	Serous	6 months	Partly intraductal papillary carcinoma Mostly undifferentiated carcinoma
D J	Bloody	0 25 month	Intraductal papillary carcinoma
M L.	Bloody	1 25 months	Intraductal papillary carcinoma
M L.	Serous	4 months	Intraductal papillary carcinoma
H H	Clear	10 months	Partly intraductal papillary carcinoma Partly moderately undifferentiated carcinoma
L. B	Bloody	36 months	Intraductal papillary carcinoma
R. E.	Bloody	1 month	Intraductal papillary carcinoma and well differentiated carcinoma
C Other Cases			
A. W	Serous	1 75 months	Circumscribed type of carcinoma Collecting nipple ducts dilated and filled with foam cells, debris, and serum
G H	Serous	23 months	Undifferentiated carcinoma. Dilated ducts containing foam cells, debris, and serum
C B	Bloody	1 5 months	Biopsy specimen only Inadequate for study
A S	Bloody	2 months	Undifferentiated carcinoma
M S	Bloody	0 5 month	No biopsy of tumor
C C.	Bloody	0 5 month	Undifferentiated carcinoma, with areas of intraductal carcinoma. Base of nipple invaded

* No palpable tumor

eroded nipple, a symptom which I have found is usually present in Paget's disease I will discuss this form of carcinoma separately in Chapter 23

Symptoms Due to Metastases

In the present chapter I have been discussing the symptoms that patients with breast carcinoma develop that lead to the recognition of their disease These symptoms for the most part, of course originate from the primary lesion In a small proportion of patients the initial symptoms are those produced by metastases

In my personal series of cases there were 13 patients whose initial symptoms related to their axillary metastases All had palpable primary breast tumors that they had not discovered Eleven complained of an axillary tumor, one of pain in the arm, and one of swelling of the arm

Pain due to vertebral metastases is another type of initial symptom of breast carcinoma The pain may be localized in the back or pelvis, or may radiate down the thigh Cohn and Cohn called attention to this clinical syndrome in a paper describing 4 cases Ducuing also emphasized the fact that bone pain, or even pathological fracture, may be the first sign of breast carcinoma

In my personal series of 546 cases there were two patients whose first symptom was back pain Both of them consulted their internist for the back pain He did a complete physical examination and found a breast tumor The story of one of these patients is worth summarizing because it illustrates the difficulty of determining whether or not back pain is due to metastases

Mrs K E, a housewife aged 51, consulted me for a breast tumor It had been discovered by her internist to whom she had gone for help concerning low back pain Her back pain had begun a year previously, but it had been increasingly troublesome during the last six months, and acute during the last month It was centered over the central lower back, and occurred almost entirely with motion Coughing and sneezing had recently produced it

She had a 5 cm tumor, with all the characteristics of a carcinoma, situated in the upper middle sector of the left breast There was a 1 cm movable left axillary node Rœntgenographic study of the lungs and skeleton showed no evidence of metastases Being aware that the back pain might be due to metastases I asked an orthopedic consultant to study her He concluded that she did not have vertebral metastases I therefore performed a radical mastectomy Three of 12 axillary lymph nodes contained metastases

Her back pain got worse during the time she was in the hospital, and became so bad after she returned home that she never really got out of bed She had to be readmitted two months after operation New x-ray studies then showed extensive metastases in ribs, pelvic bones, and lumbar vertebræ Irradiation was of little value and she died seven months after operation with widespread visceral and bone metastases

Duration of Symptoms

The length of time that elapses between the first symptom of breast carcinoma and diagnosis and treatment is an important fact The accuracy of patients' statements as to the duration of their symptoms has been questioned It is certainly true that some women are inaccurate in this regard Either faulty memory or fear may cloud their statements Individual women also vary greatly in their acuity of perception of any abnormality in their breasts I have occasionally seen women who were entirely unaware of a carcinoma involving a large part of the breast It is also true that the discovery of a tumor in the breast is usually accidental The patient's hand encounters the tumor during bathing or dressing This accidental discovery may occur soon after the tumor is large enough to detect or after it has been palpable for a considerable time If duration of symptoms is to be treated statistically as a definite point in the evolution of breast carcinoma, all these variables necessitate basing conclusions as to duration upon data from a large number of patients If this is done, however, duration certainly has some significance

Table 74 lists the average duration of symptoms in a number of large case series and indicates that even today from ten to twelve months go by before the diagnosis is made. There is some suggestion that the interval is shorter today than it was twenty-five years ago when Lane-Claypon and Harrington presented their data.

Table 74. Duration of Symptoms of Mammary Carcinoma

Author	Year of publication	Number of cases	Average duration of symptoms, months
Lane-Claypon	1926	508	20.5
Harrington	1932	4,038	17.4
Simmons, Daland and Wallace	1933	?	9.2
Nathanson and Welch	1936	575	12.1
Truscott	1947	777	10
Nohrman	1949	1,042	8.8
Bloom	1950	423	8.3
Smithers et al.	1952	797	11.2
Presbyterian Hospital Haagensen (1915–42)	Unpublished	1,420	10.7

In all ward and private patients with previously untreated breast carcinoma coming to the Presbyterian Hospital between 1915 and 1942 the average duration of symptoms was 10.7 months. The cumulated percentage distribution of these cases according to duration is shown in Table 75. From the table it is seen that approximately one half of the patients had had their symptoms for more than five months.

Table 75. Duration of Symptoms—Primary Breast Carcinomas
(Presbyterian Hospital 1915–1942)

	Number of patients	Percentage distribution (cumulated)
Under 2 weeks	117	8.2
2 weeks, under 1 month	136	17.8
1–2 months	233	34.2
3–5 months	278	53.8
6–11 months	259	72.0
12–23 months	186	85.1
24–35 months	84	91.0
36 months and over	127	99.9
Total, duration known	1420	
Duration unknown	124	
Total	1544	

One of the correlations that we have studied in our data is that between the duration of carcinomas and their size. We have used the pathologists' measurements in this study because they are presumably more accurate than the clinical measurements. Our data are shown in Table 76. They do not show a strong

correlation between duration of symptoms and tumor size—only a trend toward the concentration of the carcinomas of smaller size in the groups of patients who have had symptoms only for a short time

Table 76 Duration of Symptoms and Size of Carcinomas (Pathological Measurements) in Patients Treated by Radical Mastectomy

(Presbyterian Hospital 1915–1942)

Duration of symptoms	Under 20 mm		20-29 mm		30-39 mm		40-59 mm		60 mm and over		Total	
	No of tumors	Percentage distribution cumulated	No of tumors	Percentage distribution cumulated	No of tumors	Percentage distribution cumulated	No of tumors	Percentage distribution cumulated	No of tumors	Percentage distribution cumulated	No of tumors	Percentage distribution cumulated
Under 1 month	40	28 6	64	29 1	31	16 8	24	11 5	27	19 0	186	20 8
1–2 months	26	47 2	48	50 9	31	33 6	39	30 2	19	32 4	163	39 0
3–5 months	29	67 9	43	70 4	37	53 7	42	50 4	19	45 8	170	58 0
6–11 months	18	80 8	19	79 0	41	76 0	49	74 0	34	69 7	161	76 0
12–23 months	19	94 3	23	89 5	22	88 0	26	86 5	22	85 2	112	88 5
24 months and over	8	100 0	23	100 0	22	100 0	28	100 0	21	100 0	102	100 0
Total	140		220		184		208		142		894	

Table 77 Duration of Symptoms by Stage of Breast Carcinoma

(Presbyterian Hospital 1935–1942)

Duration	*Stage 1* Operable disease limited to breast		*Stage 2* Operable axillary nodes involved		*Stage 3* Inoperable by Haagensen-Stout criteria		Total	
	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated
Under 2 weeks	30	15 9	25	8 7	6	4 3	61	9 9
2 wks, under 1 month	23	28 1	41	23 0	9	10 8	73	21 8
1–2 months	38	48 2	43	38 0	20	25 2	101	38 2
3–5 months	38	68 3	51	55 8	27	44 6	116	57 1
6–11 months	29	83 6	41	70 1	31	66 9	101	73 5
12–23 months	16	92 1	40	84 0	21	82 0	77	86 0
24–35 months	8	96 3	19	90 6	7	87 0	34	91 5
36 months and over	7	100 0	27	100 0	18	100 0	52	100 0
Total	189		287		139		615	
Duration unknown	17		23		13		53	
Total	206		310		152		668	
Mean duration (months)	7 0		10 8		12 7		10 1	

It is interesting to analyze the relationship of the duration of symptoms to the stage of the carcinoma and to the microscopical grade of the lesion Table 77 shows the duration of symptoms by stage of disease, using our Presbyterian Hospital data for the years 1935–1942 Table 78 shows the duration of symptoms

by microscopical grade in all patients undergoing radical mastectomy during the years 1915–1942 From these data the average duration of symptoms in the different stages of carcinoma and in the different microscopical grades has been calculated

In our data the average duration of symptoms is considerably less in Stage 1 patients with operable carcinoma without axillary metastases than it is in Stage 2 patients whose disease is still operable but who have axillary involvement And the duration is almost twice as long in our inoperable Stage 3 cases as in our Stage 1 cases Nohrman s data relating duration of symptoms to stage of disease are much like ours His figures were as follows Stage 1—6 1 months Stage 2—

Table 78. Duration of Symptoms by Microscopical Grade of Breast Carcinomas Treated by Radical Mastectomy

(Presbyterian Hospital 1915 1942)

Duration	Microscopical Grade I Well differentiated		Microscopical Grade II Moderately differentiated		Microscopical Grade III Undifferentiated		Total	
	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated
Under 2 weeks	7	9 0	44	11 1	53	9 5	104	10 1
2 wks under 1 month	9	20 5	37	20 4	61	20 5	107	20 5
1 2 months	9	1 0	77	39 8	99	35 3	185	38 4
3–5 months	1	47 4	65	56	137	6_ 9	214	59 1
6–11 months	16	67 9	71	74 1	93	79 6	180	76 5
12 _3 months	8	78	59	89 0	61	90 5	128	88 9
4–35 months	6	85 9	18	93 5	4	94 8	48	93 6
36 months and up	11	100 0	6	100 0	29	100 0	66	100 0
Total	78		397		557		1032	
Duration unknown	6		5		40		71	
Total graded	84		4_2		597		1103	
Ungraded							32	
Total							1135	
Mean duration (months)	12 9		9 4		8 3		9 1	

7 6 months Stage 3—18 months Kaae reported similar findings Bloom using the Manchester system for staging also found that the proportion of advanced cases increases with lengthening delay Shimkin using Portmann s system of staging, found that the median duration of symptoms increased from four months in Stage 1 to twenty five months in Stage 4 All of these data support the reasonable assumption that as the duration of symptoms lengthens the disease advances

The microscopical grade of breast carcinoma also has a definite relationship to the duration of symptoms Our data show that the duration is longer in well differentiated, slowly growing carcinomas than in undifferentiated rapidly growing carcinomas Bloom used a plan of microscopical grading similar to that which we use and his data on this question show this same relationship These data suggest that the patients with highly malignant tumors which grow more rapidly

correlation between duration of symptoms and tumor size—only a trend toward the concentration of the carcinomas of smaller size in the groups of patients who have had symptoms only for a short time

Table 76 Duration of Symptoms and Size of Carcinomas (Pathological Measurements) in Patients Treated by Radical Mastectomy

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1–2 months	26	47 2	48	50 9	31	33 6	39	30 2	19	32 4	163	39 0
3–5 months	29	67 9	43	70 4	37	53 7	42	50 4	19	45 8	170	58 0
6–11 months	18	80 8	19	79 0	41	76 0	49	74 0	34	69 7	161	76 0
12–23 months	19	94 3	23	89 5	22	88 0	26	86 5	22	85 2	112	88 5
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(Presbyterian Hospital 1935–1942)

Duration	*Stage 1* Operable disease limited to breast		*Stage 2* Operable axillary nodes involved		*Stage 3* Inoperable by Haagensen-Stout criteria		Total	
	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated	Number of patients	Percentage distribution cumulated
Under 2 weeks	30	15 9	25	8 7	6	4 3	61	9 9
2 wks under 1 month	23	28 1	41	23 0	9	10 8	73	21 8
1–2 months	38	48 2	43	38 0	20	25 2	101	38 2
3–5 months	38	68 3	51	55 8	27	44 6	116	57 1
6–11 months	29	83 6	41	70 1	31	66 9	101	73 5
12–23 months	16	92 1	40	84 0	21	82 0	77	86 0
24–35 months	8	96 3	19	90 6	7	87 0	34	91 5
36 months and over	7	100 0	27	100 0	18	100 0	52	100 0
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It is interesting to analyze the relationship of the duration of symptoms to the stage of the carcinoma and to the microscopical grade of the lesion Table 77 shows the duration of symptoms by stage of disease, using our Presbyterian Hospital data for the years 1935–1942 Table 78 shows the duration of symptoms

siderable difference in the relationship of duration of disease to cure rates in the three different tumor grades In the well differentiated Grade I carcinomas early treatment has a clear advantage the cure rate falling from 100 per cent with prompt treatment to 62.5 per cent when treatment is delayed for between one and two years For Grade II tumors there is no significant difference in results with increasing duration But for the undifferentiated Grade III carcinomas there is again a definite advantage in early treatment the cure rate falling from 36 per cent with prompt treatment to 16 per cent when there is a delay of more than one year

Bloom has studied the significance of tumor grade upon the relationship of duration to survival in the Middlesex Hospital data He demonstrated that delay is of importance in the Grade I cases but did not find any difference in results with increasing delay in the Grade II and III cases

Table 80. Duration of Symptoms by Microscopical Grade Related to Five-Year Clinical Cure Rates Following Radical Mastectomy
(Presbyterian Hospital 1915–1942)

Duration of symptoms	Microscopical Grade I Well differentiated		Microscopical Grade II Moderately differentiated		Microscopical Grade III Undifferentiated	
	Number of cases	5-year clinical cures per cent	Number of cases	5-year clinical cures per cent	Number of cases	5 year clinical cures per cent
Under 1 month	16	100 0	81	51 9	114	36 0
1 month, under 3 months	9	77 7	77	50 6	99	36 4
3 months, under 6 months	12	75 0	65	47 7	137	35 8
6 months, under 12 months	16	75 0	71	39 4	93	29 0
1 year under 2 years	8	62 5	59	44 1	61	16 4
2 years, under 3 years	6	83 3	18	44 4	24	16 7
3 years and over	11	72 7	26	50 6	29	31 0

An interesting feature in our Table 80 is the improved clinical cure rate in patients whose carcinomas had been known to be present for three years or more We have been aware of this seemingly paradoxical fact for some time, and I am convinced that the observation is correct The explanation must be that there is a group of patients with particularly slowly growing carcinomas, who do not come for treatment until three years or more after discovery of the tumor These carcinomas, which do not fall into any special microscopical grade seem to possess comparatively less growth vigor and give a better cure rate

There must be many other factors concerned in this complex matter We are just beginning to acquire data that will perhaps eventually permit us to under stand the problem For the present the reasonable conclusion is that since it is clear that early treatment gives better results in at least some breast carcinomas and since we cannot very well as yet identify these more curable carcinomas

come for treatment sooner, perhaps because the rapid rate of growth alarms the patient

It is when we attempt to correlate the duration of symptoms with the results of treatment that we encounter conflicting opinions In their 1951 paper that has been so much debated Park and Lees could not demonstrate in their data any advantage in early diagnosis and treatment Their data, however, had several important defects In the first place, the information as to duration of disease in the Edinburgh case histories was often indefinite according to Park and Lees themselves, and they had to estimate what the duration actually was More important, their data included only the cases operated upon The advanced inoperable cases were omitted The information concerning these neglected advanced cases is certainly pertinent to the question of the advantage of early diagnosis and treatment

From our Presbyterian Hospital data we are able to present a correlation of duration of symptoms and five year clinical cure rates (Table 79) that gives a

Table 79. Duration of Symptoms Related to Five-year Clinical Cure Rates—All Primary Breast Carcinomas

(Presbyterian Hospital 1915–1942)

Duration	Number of cases	Five-year clinical cures	
		Number	Per cent
Less than 1 month	253	106	41 9
1 month, under 6 months	511	181	35 4
6 months, under 12 months	259	74	28 6
1 year, under 3 years	270	68	25 2
3 years and over	127	33	26 0
Duration not definitely stated	124	45	36 3
Total	1544	507	32 8

somewhat different impression from Park and Lees' data Our data are based upon some 1,500 carefully taken case histories, and include all primary cases, whether they were treated or not Our data show a seeming decrease in the clinical cure rate with increasing duration of disease For patients with symptoms of less than one month's duration the five year clinical cure rate was 41 9 per cent The cure rate fell as duration increased to reach 25 2 per cent in patients who had had symptoms for between one and three years

Shimkin calculated from his data relating duration of symptoms to survival, that if all his patients had come for treatment within a month after onset of disease the five year survival would have been 60 per cent instead of the 40 per cent that was actually observed This is a solid argument against the nihilism of those like Park and Lees, and McKinnon, who see no advantage in early diagnosis

In pursuing the question of the relationship of duration of symptoms to results of treatment it is worth while to study the significance of the microscopical grade of malignancy Table 80 shows this correlation in our Presbyterian Hospital data Since this correlation is based upon microscopical evidence as to the tumor grade only the operated cases can be included in it, for the inoperable lesions were not all biopsied and graded It will be seen that there is a con-

afraid They are afraid of doctors and hospitals of operation and of cancer itself as they have observed its course in friends and relatives It is not enough therefore to educate people as to the symptoms of cancer Their fear of the disease must be overcome by convincing them that it can be cured

Table 82. Duration of Primary Symptoms in Carcinoma of the Breast Ward Patients
(Presbyterian Hospital 1935–1942)

Length of time	Number of patients	Percentage (cumulated)
Under 2 weeks	24	6 0
2 weeks—less than 1 month	37	15 3
1–2 months	58	29 9
3–5 months	87	51 8
6–11 months	74	70 4
12–23 months	57	84 7
24–35 months	24	90 7
36 months or over	37	100 0
Total	398	
Average delay	11 1 months	

My own experience in studying the cause of delay in my patients has long since convinced me that fear is indeed the chief deterrent to earlier diagnosis Propaganda to overcome fear is particularly difficult, but I believe that, in general truth is the weapon that is most useful We must make a special effort to bring the subject of cancer out into the open to make it a respectable disease, and to emphasize the good results of treatment in the favorable types of cancer

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preoperatively, we had better strive for earlier recognition and more prompt treatment of all breast carcinomas

Reasons for Delay

If we knew why women with symptoms of breast disease delay seeking medical advice we might be able to do something about getting them to come earlier Our data indicate that the duration of symptoms has a close relationship to the financial or social status of the patients In my series of 546 personal cases, which includes a higher proportion of women of good education and adequate financial means than our Presbyterian Hospital series of ward cases, the average interval between the first symptom and the diagnosis was 7 5 months This is the shortest average duration of symptoms yet reported from an American clinic, to my knowledge The cumulated percentage distribution of my personal cases according to duration is shown in Table 81 From this table it will be seen that one-half

Table 81 Duration of Primary Symptoms in Carcinoma of Breast Personal Series (1942–1955)
(1942–1955)

Length of time	Number of patients	Percentage (cumulated)
Under 2 weeks	85	17 2
2 weeks—less than 1 month	56	28 5
1–2 months	120	52 7
3–5 months	76	68 1
6–11 months	61	80 4
12–23 months	51	90 7
24–35 months	22	95 1
36 months or over	24	99 9
Total	495	
Average delay	7 5 months	
No symptoms Disease discovered at physical examination	51	
Total	546	

of the patients had had their symptoms only two months or less The average duration of symptoms in our Presbyterian Hospital ward patients (1935–1942) was 11 1 months The cumulated percentage distribution of these ward cases is shown in Table 82 Only about one-third of the ward patients had had their symptoms for two months or less

Without doubt one of the most important reasons for delay is fear Here both education and moral courage play a role, but it is difficult to assess their relative importance Aitken-Swan and Paterson have recently made a careful and penetrating analysis of the question in a series of 127 patients with breast cancer They found, first of all, that 72 per cent knew that their symptoms might mean that they had cancer Of this group, who "knew" the significance of their symptoms 65 per cent nevertheless delayed more than three months in seeking help This group of patients, Aitken-Swan and Paterson point out, is the chief challenge to any effort at public education concerning cancer These patients know that cancer threatens them but they delay going to a physician because they are

CHAPTER 21

THE DIAGNOSIS OF BREAST CARCINOMA

In Chapter 5 I described the methods of breast examination and the biopsy procedure I use to diagnose breast lesions in general These methods are of course applied in diagnosing carcinoma In the present chapter I wish to discuss certain special aspects of the problem in differential diagnosis that carcinoma presents

It might be well to begin with an analysis of how the diagnosis was made in my personal series of 546 cases of breast carcinoma (1943–1954) Because I took these case histories myself they are perhaps more complete than those for our Presbyterian Hospital ward patients taken by interns

Breast Carcinoma Found at Routine Physical Examination

In 50 of the patients or 9 2 per cent the disease had been found by a physician *during a physical examination The patients had had no symptoms referable to* the breast and were unaware of their breast disease In one additional patient the breast tumor had been found by a nurse bathing her patient.

This is a higher percentage of patients in whom the disease was unexpectedly discovered at physical examination than in our previously published Presbyterian Hospital data (1915–1945) where the incidence of carcinomas found at physical examination was 5 9 per cent. In the Presbyterian Hospital series most of the patients were from the ward service It might be supposed that the private patients in my personal series would have had physical examinations more often than ward patients and therefore a better chance of having carcinomas found in this way

I must point out, however that the frequency with which physicians find carcinoma of the breast at physical examination of patients with no breast symptoms is directly proportional to their skill in examining the breast. Some physicians who are not much interested in the problem of breast disease and who examine the breast inadequately never seem to find breast carcinomas On the other hand I know two physicians, one an internist and the other an obstetrician, who have been specially interested in breast carcinoma and are unusually expert in breast examination each of whom has found two or three unsuspected breast carcinomas every year Almost all of the carcinomas that they have found have been small and curable Gynecologists and obstetricians have, of course, an exceptional opportunity to examine the breast but not all of them take advantage of it

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Diagnostic Errors Made by Physicians

The remaining 496 patients in my personal series of cases came to physicians with signs or symptoms due to breast disease which they had themselves noted In 115 patients, or 23 per cent, the diagnosis was at first missed, and wrong medical advice or treatment given I have classified as wrong advice and treatment only such recommendations as all would agree to be obviously incorrect for carcinoma In 22 of these 115 cases two or more physicians erred

I have attempted to analyze these errors by classifying them as follows

1 *Failure to examine a breast containing an obvious tumor while treating the patient for an unrelated disease* The story of a recent patient illustrates this kind of error

Mrs A I , a housewife aged 60 was admitted to the hospital for cardiac disease and a tumor of the breast She had had heart trouble for fifteen years, requiring digitalis and, during recent years, mercurial diuretics She had been under the constant care of her local physician, who had examined her at least every two weeks and prescribed diuretics for her dyspnea and edema Six months previous to her admission to our hospital, she had discovered a tumor of her right breast She had not told her local physician about it, and since he had not examined her breasts on the many occasions when he had examined her heart, he had not found it

She had an obvious 3 cm carcinoma of the lower outer sector of her right breast Because of her marginal cardiac reserve we chose to treat her with irradiation

This error can be avoided to a degree by physicians examining the breasts as part of the general physical examination that they give every new patient As Root has pointed out, however, when old patients, who are also old friends, drop in to a physician's office for a minor complaint, it is not easy to insist upon a general physical examination The way to avoid missing something new in old patients is to follow the rule of doing a general physical examination, including examination of the breasts, at least every six months

2 *Failure of the physician, in his palpation of the breast, to feel the tumor that the patient had discovered and for which she came to consult him*

This mistake is illustrated by the experience of Mrs C D , aged 42, who happened to palpate her left breast as she lay in bed and discovered a small tumor in it She went at once to her family doctor and pointed it out to him He examined her breast but could not feel the tumor He told her that there was "nothing wrong with her breast" and that she was "just nervous " He gave her "medicine to settle her nerves "

Six months later, the tumor persisting, she came to consult me Her tumor, which was situated in the lower outer sector of the breast, was 2 cm in diameter and entirely typical of a carcinoma

This is the most difficult diagnostic error to avoid, because it depends upon palpatory skill, and not upon following rules It is an all or none kind of error If the patient has a tumor it must be investigated, but if no tumor can be felt, she is dismissed

3 *Mistaking a carcinomatous tumor of the breast for a breast infection* This kind of mistake is perhaps more frequent since the discovery of antibiotics It was made in the case of Mrs L H , aged 64

Four months before she came to consult me she had noted that her left nipple was becoming retracted A month later she discovered a lump in the breast Two months later the skin over the breast became red and hot and she consulted her family doctor He diagnosed the lesion as an infection and prescribed sulfadiazine and ice packs to the breast With this treatment the inflammatory symptoms gradually disappeared but the tumor persisted and she came to me for another opinion

She had a large 10 cm. carcinoma with axillary metastases 2 5 cm in transverse diameter The redness had disappeared but limited edema of the skin remained

This error can of course be avoided by biopsy The existence of disease is obvious Only its nature remains to be proved

4 *Wrongly diagnosing a carcinomatous tumor of the breast as a benign lesion and failing to advise biopsy or excision*

A good example of this kind of error was found in the case history of Mrs. G M aged 44 a physician s mother in law who consulted me for a tumor of her breast that she had discovered 24 months previously while bathing She had at once called it to the attention of her family doctor He regarded it as benign and advised her to do nothing about it. He had been giving her weekly injections of estrogen for the previous two years because her menses had been irregular and he continued this hormone therapy for a year after Mrs M had consulted him for her breast tumor The tumor persisting, four other physicians—a surgeon an internist a gynecologist and an otolaryngologist—were consulted regarding it All diagnosed it as a cyst and advised no treatment.

The tumor nevertheless continued slowly to enlarge When I saw Mrs. M it measured 5 cm in diameter and although it was well delimited and comparatively movable in the breast like a cyst it was hard and there was slight dimpling of the skin evident in the forward bending position At biopsy it proved to be a carcinoma

This kind of error can be avoided by following the simple rule of surgically proving the nature of every dominant tumor of the breast

5 *Disregarding a history of acute and sharp pain in the breast* The following case illustrates the fact that even this infrequent symptom of breast carcinoma should not be ignored

Mrs. R. K., aged 56 first developed a "sticking" pain in her right breast six months previously while in another hospital for a minor gynecological operation She could not feel any tumor in her breast. She called the attention of her gynecologist to the breast pain and he told her that it was nothing." After she returned home from the hospital the sticking pain recurred and she consulted two local physicians regarding it. The first told her that the pain was due to "a muscle strain" and gave her a salve The second told her she had "hardening of the arteries." She finally went to a public clinic from which she was sent to me

I found that she had a small 2 cm carcinoma in the upper outer sector of the breast —the region in which she had had the pain.

This error can be avoided by careful palpation of the breast in which the pain is centered

6 *Disregarding a definite retraction sign* A good example of this kind of error was the case of Mrs F F aged 52.

Three years before she came to consult me she had noticed a dimple in the lower portion of her left breast. She consulted her family physician about it. He said it was

Personal Diagnostic Errors

While pointing out the errors made by other physicians in the diagnosis of breast carcinoma I must not fail to point out my own In the series of 546 personal patients with breast carcinoma to which I have referred I failed to diagnose carcinoma in four Three of my errors were of one type—failure to feel the breast tumor and dismissal of the patient In the fourth patient I delayed too long in a patient with nipple discharge but no tumor The details of these four cases follow

Case 1 Mrs M O a housewife aged 45 came to the Presbyterian Hospital in March 1944 complaining of a tumor in the upper outer sector of her right breast that she had discovered while bathing She had large dense dependent breasts I examined her with care and failed to find the tumor I dismissed her and worst of all I failed to ask her to return for repeated examination

She returned of her own accord 9 months later in January 1945 again complaining of the breast tumor This time I found the tumor It was a small 2 cm firm poorly delimited mass situated deeply in the upper outer sector of the right breast It was easier to feel with the patient sitting up than in the supine position The lesion was biopsied and proved to be a carcinoma Radical mastectomy was performed The carcinoma measured 1 cm in diameter grossly Metastases were found in one of 9 axillary lymph nodes. The patient fortunately is well ten years later

Case 2 Miss F W a 37 year-old stenographer consulted me in March 1949 because she had begun, in January to have pain in her right breast It was centered in the outer portion of the breast varied in type and was accentuated during menstruation. In February she had become aware of a diffuse barely palpable induration in the upper outer portion of the breast

In my examination in March I found her right breast to be rather dense, but I did not make out any dominant tumor I dismissed her and again made the error of not asking her to return for examination

She returned in July with a 6 cm. firm poorly delimited tumor filling the outer middle sector of the breast There was faint redness of the skin over the tumor and a small area of edema of the skin caudad to it. There were several linear areas of retraction in the skin over the tumor In the axilla there were several 0 5 cm to 1 cm. hard nodes

At biopsy the lesion proved to be a carcinoma. Radical mastectomy revealed a 6 cm. undifferentiated carcinoma, with tumor emboli in veins and lymphatics, and metastases in 16 of 23 lymph nodes including the highest or subclavicular nodes.

She developed right supraclavicular metastases in October pulmonary metastases in December and died in March 1950 a year after I had missed her carcinoma.

Case 3 Mrs E. H a widow aged 59 was sent to me in April 1954 by her physician who had found in the course of a routine physical examination, a small tumor of her left breast of which the patient was entirely unaware.

In my examination I failed to find a tumor The patient was vague as to how the supposed tumor had been found and as to its position in the breast I further failed to insist upon learning her physician s name and checking the discrepancy in our findings by talking with him

She went back to her physician who had the good sense to send her back to me asking me to re-examine her When I did so in June I found the tumor but only after she had pointed out its location to me. It was situated in the radius of 5 o clock of the left breast, about 2 cm beyond the areolar edge It measured less than 1 cm. in diameter but it was firm and poorly delimited. There was a definite slight dimple in the skin over it when the arm was raised I could feel the tumor easily when the patient sat up but when she lay supine it disappeared into the soft subareolar breast tissue

At biopsy it proved to be a carcinoma Radical mastectomy showed metastasis in one of 18 axillary lymph nodes

Case 4. Mrs A S , a housewife aged 53, consulted me in February, 1952, because she had occasionally noted a spot of blood on the left side of her brassiere during the previous 2 months

I examined her left breast with care, giving special attention to the central subareolar area, but I could not make out any tumor Neither could I find any pressure point that would produce the nipple discharge I advised surgical exploration if and when the site of the presumed papilloma could be localized by repeated examination, and suggested that she return in three months for reexamination

She did not come back to me but went to another physician after this period of time He found that she had an undifferentiated carcinoma with axillary lymph node metastases

In analyzing these diagnostic errors of my own the main conclusion that I draw is that I should have paid closer attention to the patients' own findings in self-examination When the patient says she has a tumor I must always use her help in defining its exact location and character If I nevertheless fail to identify a tumor, I must not dismiss her, but reexamine her at no more than a month's interval In the fourth patient in whom I delayed too long advising surgical exploration when there was a bloody nipple discharge but no tumor or other indication of the site of the lesion, I clearly failed to follow the rule that such patients must have prompt surgical investigation I will discuss this special diagnostic problem separately, later on in the present chapter

Long Delay in Patients in Whom the Diagnosis Was Missed

In the 115 patients in my personal series of cases in whom the diagnosis was initially missed by one or more physicians, the added delay in correct diagnosis and treatment that must be charged to the physicians' errors was distressingly long It averaged 12 5 months During this relatively long period of delay due to physician failure the disease must have progressed to the point of incurability in a good many of the 115 patients It is a heavy responsibility that we, as physicians, bear in the diagnosis of lesions of the breast We must improve our medical education in regard to the diagnosis of breast lesions Each one of us must also set for himself the highest standard of exactitude in the diagnosis of lesions of the breast, always seeking to improve our personal clinical skill and to discipline it by the pathological diagnoses in our patients

There are several special types of breast carcinoma that present unusually difficult diagnostic problems I will discuss each of them individually They are *occult breast carcinoma*, *carcinoma of the axillary prolongation of the breast*, and *carcinoma producing a nipple discharge but no palpable tumor*

Occult Carcinoma of the Breast

There are rare mammary carcinomas in which there is no palpable tumor in the breast nor any symptom of disease in the breast such as pain or nipple discharge In this sense these carcinomas are occult

These patients usually present themselves with an axillary tumor, which when biopsied proves to be metastatic carcinoma in a lymph node Palpation of the breasts fails to reveal any tumor, and no other source for the metastasis can be found In this dilemma some surgeons have performed radical mastectomy, assuming that there must be a small and occult carcinoma hidden in the breast,

and have actually found one Other surgeons have preferred to observe the patient and eventually after a period of time which may be as long as several years, the primary lesion in the breast becomes evident as a definite tumor

Halsted a great expert in the diagnosis of breast carcinoma as well as the originator of our modern operation was the first to write of occult carcinoma of the breast In his 1907 paper he described 3 cases What he wrote is worth quoting I have twice seen extensive carcinomatous involvement of the axilla due to mammary cancer which latter in neither instance became palpable or demonstrable for a considerable period after the axillary glands had attained conspicuous dimensions In each case the axillary tumors had been removed in one of them a year before and in the other perhaps two years prior to my first examination which though made in the most careful manner failed to find the slightest evidence of cancer of either breast In the course of a few months thereafter the mammary disease manifested itself in both patients

"A third patient was operated upon for enlarged glands of the axilla about two and one-half years before she consulted me concerning the local axillary recurrence of the disease and more especially to be relieved of severe neuralgic pains in the arms and legs. In this woman I found a large mass of axillary glands which proved to be cancerous but nothing in the breast except a quite definite parchment like induration at the base of the nipple which was retracted not at all or merely to a barely appreciable degree.

During the last few years there has been a flurry of papers regarding occult breast carcinoma Good case reports have been presented by Rawls Jackson Cogswell Rutkowski Klopp Fitts and Horn Weinberger and Stetten Rabinovitch Huguet, Davidoff Kaplan and Reinstine Roux Berger discussed the problem which these cases present and emphasized the long delay in diagnosis that usually occurs

Another clinical form in which occult breast carcinoma manifests itself is as distant metastases in bone or viscera without an accompanying palpable tumor of the breast The primary lesion is found only at autopsy Horwitz, and Fitts and Horn described cases of this type.

Until Owen Dockerty and Gray recently studied the question in the records of the Mayo Clinic there has been no estimate of the frequency of occult carcinoma of the breast. Among 5 451 cases of breast carcinoma, they found 24 or 0 3 per cent, in which there was no breast tumor and no nipple discharge The presenting symptom in these cases was an axillary tumor which proved on biopsy to be metastasis in lymph nodes Radical mastectomy was then performed and an occult primary carcinoma found in the breast.

At the Presbyterian Hospital we have had three occult carcinomas of the breast among approximately 1 600 patients with mammary cancer The first two of these cases are examples of the wisdom of radical mastectomy in the presence of axillary metastases, even though no tumor was felt in the breast. The third case is a remarkable example of the slow evolution of the primary tumor in the breast Summaries of these cases follow

Case I Mrs. G S a housewife aged 54 was admitted to the Presbyterian Hospital, complaining of a tumor of the right axilla that she had had for 3 months. The axillary

Case 4. Mrs A S, a housewife aged 53, consulted me in February, 1952, because she had occasionally noted a spot of blood on the left side of her brassiere during the previous 2 months

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radical mastectomy was done for presumed occult breast carcinoma no carcinoma was found in the breast In all fairness to the patient this possibility should be explained to her if she is advised to have radical mastectomy under these circumstances

Carcinoma in the Axillary Prolongation of the Breast

Another difficult type of breast carcinoma to diagnose is that arising in the axillary prolongation of the mammary gland As I pointed out in Chapter 1 a good many women have such axillary mammary tissue When carcinoma develops in it, the tumor is usually mistaken for lymph node disease Mornard Piccagli Dickinson and Stringa have described cases of carcinoma arising in axillary mammary glands

In the Presbyterian Hospital records we have two cases of this kind One of them is worth summarizing

Mrs U M a colored housewife aged 41 was admitted to the Presbyterian Hospital for a tumor of the left axilla She was three months pregnant She had first noted the axillary tumor fifteen months previously during a pregnancy that ended in a miscarriage During the five months prior to her admission the axillary tumor had gradually increased in size

Examination showed a stony hard irregularly nodular tumor of the left axilla, measuring 4 x 6 cm It was fixed to the deeper axillary structures and to the overlying skin. The skin attachment is shown in Figure 262. No tumor was palpable in either breast

The axillary mass was excised and was found to be a carcinoma measuring 5 x 4 cm. arising in axillary mammary tissue. At the upper pole of the axillary specimen there were several large lymph nodes containing metastases. Radical mastectomy was performed. No carcinoma was found in the breast removed by the mastectomy

The patient received postoperative irradiation to the operative field and the supraclavicular area, and ovarian irradiation. She shortly miscarried Twelve months after operation however local recurrence on the chest wall developed and she died with widespread metastases to bones after another two years.

Carcinoma Producing a Nipple Discharge but No Palpable Tumor

When a patient with a nipple discharge also has a breast tumor or when a point in the breast can be found upon which pressure produces the nipple discharge thus localizing the breast lesion and making it possible to place the exploratory incision in the appropriate sector of the breast, there is no doubt about what to do The lesion should at once be investigated surgically

But when there is no palpable tumor and no pressure point can be found the surgeon s dilemma is a difficult one If he explores the breast blindly and makes his circumareolar incision on the wrong side of the areola opposite to that in which the diseased ducts are situated he may not find the papilloma or the small carcinoma responsible for the nipple discharge Surgeons of a generation ago could put off such patients and wait until the site of the lesion in the breast could by found by reexamination for Hart, who had written one of the best papers on nipple discharge had stated that in his Johns Hopkins data there was no case of breast carcinoma with a nipple discharge but no accompanying breast tumor

Today unfortunately we know that such cases although rare, do occur Fitts and Horn have recently described 4 cases of breast carcinoma in which there

mass was 6 cm in diameter, firm, and freely movable No tumor could be found in the right breast Dr J M Hanford biopsied the axillary tumor Finding it to be carcinoma on frozen section, he proceeded with radical mastectomy In the gross study of the operative specimen no carcinoma was identified But one of fourteen microscopical sections cut from cystic or firm areas in the breast, none of which was more suggestive of carcinoma than any other, revealed a minute focus of carcinoma The axillary metastases formed a 5 cm mass of fused nodes The patient died with generalized bone and visceral metastases four months postoperatively

Case 2 Mrs M P , a widow aged 66, came to the Presbyterian Hospital, because of a tumor of the left axilla that she had discovered two weeks previously

In her left axilla there was a very large, firm tumor fixed to the skin as well as to the deeper tissues of the axilla It measured 8 x 5 cm No tumor could be identified in the breast by Dr Hugh Auchincloss, whose patient she was, or by several other examiners

The axillary mass was first excised for diagnosis and was found to consist of two lymph nodes largely replaced by metastatic carcinoma The larger measured 4 5 cm and the smaller 1 2 cm in diameter Dr Auchincloss then went ahead with radical mastectomy On sectioning the mastectomy specimen a 1 cm primary carcinoma was found in the upper outer sector of the breast Sections of fifteen axillary nodes dissected from the mastectomy specimen showed no metastases Although the carcinoma was undifferentiated in type, the patient is well thirteen years after operation

Case 3. Mrs C B , a nurse aged 48, was admitted to the Presbyterian Hospital, for treatment of a tumor of the left axilla of two months duration Her past history was significant only in that twelve years previously a single cyst, 2 cm in diameter, had been excised from just above the areola of her left breast

In the lower left axilla there was a round, movable, 6 cm tumor The breast was examined by three of our surgeons specially skilled in the diagnosis of breast disease, none of whom could find a tumor I also examined it and found nothing abnormal The axillary tumor was excised locally and was found to consist of three encapsulated lymph nodes measuring 6 cm , 5 cm and 3 cm , respectively In all three the lymphoid tissue was almost entirely replaced by carcinoma, which resembled breast carcinoma Although we recommended radical mastectomy on the grounds that there was probably an occult carcinoma in the breast, the patient demurred and we did not press the matter

The patient's breasts were examined regularly by a skilled examiner, but it was not until five years and four months after the axillary metastases had been discovered that a tumor was found in the left breast It was situated in the radius of 2 o'clock, about 6 cm out from the areolar edge It measured 2 cm in diameter, and had the firm, poorly delimited character of a carcinoma

I biopsied the breast tumor, which lay deep in the substance of the breast, proved it to be a carcinoma, and performed a radical mastectomy Study of the operative specimen showed the primary tumor to be only 1 cm in diameter It was a moderately undifferentiated carcinoma There were no metastases in 19 lymph nodes

The inescapable fact in this case is that it took more than five years for the occult breast carcinoma to grow to a diameter of 1 cm and become palpable, after it had given rise to large axillary metastases

It is easy in retrospect to argue that all patients like this one, with metastatic axillary carcinoma and no palpable breast tumor or other primary source for the metastases, should have radical mastectomy But we cannot ignore the fact that if the operation is done no carcinoma will be found in the breast in a considerable proportion of the cases Jackson, who wrote one of the best earlier papers on the subject, pointed out in the discussion of Cogswell's subsequent report that he had had this experience Owen, Dockerty and Gray admitted in their review of the Mayo Clinic experience that in 10 patients, or 30 per cent of those in whom

It was severed at the base of the nipple and a cone of breast tissue surrounding it excised. The gross study of the specimen revealed a friable, soft, yellowish tumor in the proximal portion of the dilated duct. The microscopical sections showed that there were multiple benign papillomas in several of the ducts and in one intraductal carcinoma.

Right radical mastectomy was done a week later No residual papilloma or carcinoma was found in the specimen and no metastases were found in 26 lymph nodes.

Eighteen months later Dr Habif in his examination of the patient, found a 5 mm tumor in the left breast. It was situated 2 cm from the areolar margin in the radius of 10 o clock There was dimpling of the skin over the tumor in the forward bending position. The tumor was excised and showed the same lesions as had been encountered in the right breast, benign intraductal papilloma and intraductal carcinoma. Since the patient was 71 and her breast disease was not regarded as much of a threat to her left complete mastectomy only was done. In the amputated breast diffuse benign intraductal papilloma, but no more carcinoma, was found

My experience in these cases has forced me reluctantly to the conclusion that in patients with a spontaneous nipple discharge a surgical search for the lesion must be carried out with reasonable promptitude even though there is no palpable tumor or pressure point to indicate the site of the disease The great majority of these patients without localizing signs will have benign intraductal papilloma and the surgical search for the papilloma will be greatly handicapped if it has to be attempted without any indication as to the radial position of the lesion in the circumareolar region In order to minimize the number of cases in which exploration has to be done without such localizing information I suggest the compromise of deferring operation a month and examining the patients at weekly intervals during this period searching for a pressure point that will betray the radial site of the lesion In the rare lesion that proves to be a carcinoma one month s delay will not add greatly to the hazard while the task of finding the papillomas that produce the discharge in most of the patients will often be simplified by the localizing information found by repeated examination. Delay longer than one month is however unwise, for the possibility that the cause of the nipple discharge is carcinoma is remote but real

In occasional cases the clinical circumstances in a patient with a history of spontaneous nipple discharge are such that surgical exploration is not reasonable. The following is such a case

Mrs. G L. a housewife, age 40 was sent to me in November 1949 Her history was that since the age of 20 she had occasionally had slight bloody discharge from the nipples of both breasts. The discharge was sufficient to stain the sheets and her brassiere. From the age of 37 on, the discharge had almost completely disappeared. She came to consult me because within the last month the discharge had begun again, this time from the right breast, from which there had been an occasional drop of dark blood.

On examination her breasts were normal. I could not make out any tumor in either breast. I could find no pressure point which would produce the discharge.

She has been followed at intervals and no tumor has developed in either breast. The discharge has disappeared. There was no evidence of disease in her breasts in January 1955 more than five years after I first saw her

A phenomenon that is not an indication for surgical exploration is the slight bloody nipple discharge that occurs from both breasts in some pregnant women This is an expression of the intensity of the epithelial proliferation in the rapidly

was a nipple discharge but no breast tumor Kilgore and his associates also refer to four such cases that they observed, but they describe only one of them In my own personal series of 546 patients with carcinoma there were 21 with a nipple discharge In 2 of these patients there was no palpable breast tumor

In one of these patients I postponed surgical exploration too long I have already summarized her history in my account of my personal diagnostic errors She had a bloody nipple discharge but no tumor and no pressure point



Fig 262 Carcinoma of the axillary prolongation of the breast

The other patient, Miss M B, a spinster aged 69, consulted me because of a discharge from the right nipple Ten months previously she had fallen and struck her breast slightly Shortly thereafter she noted on two occasions a few drops of blood spotting her nightgown opposite her right nipple This had recurred recently and led her to consult me

Her breasts were symmetrical and no tumor was palpable in either one On palpation of the right circumareolar region a pressure point was found at the radius of 8 o'clock which produced a drop of brown serous discharge from a duct in the center of the right nipple Prompt surgical exploration was advised

She was operated upon by my associate, David Habif Through a circumareolar incision the collecting ducts leading to the base of the nipple from the outer sector of the breast were exposed One of them was seen to be dilated and filled with dark blood

An excellent review of the literature on the problems of steroid metabolism in patients with cancer has been written by Engel

Duct Ectasia Simulating Carcinoma

The most difficult lesion to distinguish from carcinoma of the breast because of the marked degree of fibrosis and the resulting retraction signs which it produces, is duct ectasia I have described its characteristics in Chapter 10 but wish to emphasize again here that it is clinically indistinguishable from carcinoma Among all the lesions that occur in the breast it is the most likely to deceive the clinician into thinking that he must be dealing with a carcinoma and that it is safe to go ahead with radical mastectomy without a biopsy The occurrence of this deceptive lesion in the breast is sufficient ground in itself to make it necessary always to perform a biopsy before carrying out mastectomy

There are one or two features of duct ectasia which may suggest its presence One is the fact that the tumor of duct ectasia usually lies in the central area of the breast beneath or close to the areola A second point is that the signs of inflammation which evolve with this lesion are less acute than with an ordinary breast abscess and more localized than with inflammatory carcinoma. Finally the disease unlike an ordinary abscess often occurs in women who have not recently lactated

Lymph Nodes Within the Breast Area

In a number of patients I have biopsied a small tumor of the upper outer sector of the breast which I thought was a lesion of the breast itself either a cyst or a carcinoma, and found that it was only an enlarged lymph node. The breast tissue normally extends laterally across the lower portion of the anterior axillary fold, and in women with good sized breasts this upper outer margin of the breast may be rather thick Occasionally an enlarged lower axillary lymph node will be found situated low along the edge of the pectoral fold or near the edge of the pectoral fold upon the ventral surface of the pectoralis muscle, seemingly well within the limits of the upper outer sector of the breast Such a lymph node, when covered by breast tissue, feels firm and only moderately well-delimited It cannot be distinguished clinically from a tense cyst or a small carcinoma.

Metastatic Tumors of the Breast

Even though a breast tumor is malignant, and of epithelial origin the possibility of its being a metastasis to the breast from a primary carcinoma in some other site must be kept in mind This sequence is rare Dawson collected reports of ten such cases and added one an example of metastasis of carcinoma of the stomach to both breasts. Speert and Greeley and Schumann described individual cases and Charache has recently reported six others

I have studied one patient with a metastatic tumor in the breast Her story was as follows

Mrs. H M a housewife aged 39 developed a non-productive cough and weakness When she came to the Presbyterian Hospital ten weeks later two lesions were found—a hard 2 cm. fixed mass in the left lobe of the thyroid and a 5 x 8 cm. oval shadow with well defined margins just below the middle of the left lung.

growing breasts There were two such patients among the 117 in my personal series of patients with a nipple discharge to whom I have referred A milky secretion continuing long after lactation is apparently over is of course another physiological phenomenon that does not require surgical investigation

General Diagnostic Rules

Although I invariably perform knife biopsy to prove the nature of a breast lesion before carrying out any radical treatment, it is helpful for many reasons to develop as high a degree as possible of clinical skill in differentiating carcinoma from other breast lesions The time and convenience saved in planning operative schedules by being able to guess the diagnosis fairly accurately is alone a sufficient reason for cultivating diagnostic skill

I have discussed the clinical characteristics of most of the lesions of the breast in the preceding chapters, and all I can do at this point is to suggest some general rules that may help in differential diagnosis

One of these rules is that the smaller the primary tumor, the more difficult its clinical diagnosis Carcinomas 1 cm or less in diameter may not produce an appreciable degree of retraction, and they are very difficult to distinguish from cysts, adenosis, fibrous disease, etc I have learned to be very cautious about predicting the nature of the very small breast lesions Larger carcinomas are usually betrayed by their lack of delimitation, their relative fixation in the breast tissue, and the retraction that they produce

Another sound rule is that the older the patient the more likely breast carcinoma After the menopause, when cysts no longer develop, the comparative frequency of carcinoma rises sharply

Finally, carcinoma is considerably more frequent in women who have a family history of breast carcinoma as well as in those who have had cystic disease, as I have indicated in Chapters 17 and 7 These facts have some weight in making a tentative differential diagnosis

Diagnostic Tests for Breast Cancer

Unfortunately, there is no laboratory test, excepting, of course, microscopical study of tissue, that enables us to recognize carcinoma of the breast Much clinical evidence suggesting that the steroid hormones play a part in the origin and growth of the disease has accumulated during recent years Many efforts have been made to ascertain quantitative differences in ketosteroid excretion between normal individuals and patients with breast cancer None of these has revealed that the over-all excretion of these substances is abnormal in patients with breast carcinoma There have been some reports, such as those of Nathanson and Engela and Segaloff and Gordon, which suggest that patients with breast carcinoma metabolize exogenously administered steroids differently from patients without cancer, and also that these cancer patients respond differently to the administration of ACTH Although these experiments suggest the existence of different metabolic pathways in cancer patients, much additional work will be required before the significance of these experiments can be determined

inframammary region diagonally downward toward the epigastric or hypochon dnal region The cord stands out sharply when the arm is raised It lies just beneath the skin which is fixed to it When crossing the softer breast tissue it forms a furrow The lesion may be so painful as to cause dyspnea as in Williams case Microscopical studies of the lesion by Hughes and by Lunn and Potter show that it consists of thrombosis of a subcutaneous vein followed by thicken ing of the vessel wall and a surrounding zone of fibrosis The vein or veins affected are good sized subcutaneous veins which normally cross the lateral chest region and breast from the epigastric or hypochondriac region to the axilla The disease is self limited subsiding after a few weeks Its etiology is unknown It appears to have no relationship to disease in the breast although in one of Lunn and Potter s 5 cases there was a coexisting carcinoma of the breast About half of the reported cases have been in males

I have myself studied 4 patients with subcutaneous phlebitis of the breast region and we have one additional case in our hospital records My 4 patients were all women None of them had any apparent breast disease In 2 the cord like thickening extended from the lower axilla just behind the anterior axillary fold downward to the lateral aspect of the breast. In the third patient the lesion extended from the lateral inframammary area downward across the hypochon drium In the fourth patient the furrow caused by the lesion cut across the lower outer sector of the breast (Fig 263) I did not biopsy the lesion in my patients because I was familiar with its nature No treatment was given In all 4 patients the lesion disappeared spontaneously after a few weeks

Summary

The price of skill in the diagnosis of breast carcinoma is a kind of eternal vigilance based upon an awareness that any indication of disease in the breast may be due to carcinoma The physician s sympathy with a patient s distress the *seemingly benign physical character of a breast lesion a natural desire to avoid* all the hard work that goes into dealing with a carcinoma—all conspire to lull the physician into a state of mind in which he tends to think of the lesion as benign The only way to avoid this kind of error is to follow the strict rule of always explaining to the patient that the clinical evidence is not final, and that the definitive diagnosis is based upon the microscopical findings after biopsy She must always be told of the possible necessity of radical mastectomy and must give her approval All of these preparations, if they serve no other purpose, keep the surgeon alert to the threat of carcinoma.

The likelihood of the disease being present steadily increases with the age of the patient, and is comparatively much greater after the menopause when cysts no longer develop The diagnostician should also keep in mind the fact that carcinoma is about four times as frequent in women who have had cystic disease, and in those who have a familial history of breast carcinoma as it is in the general female population

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The thyroid tumor was biopsied and proved to be a poorly differentiated primary thyroid carcinoma It was assumed that the lung lesion was a metastasis and irradiation to both the thyroid and the lung lesions was begun

Two months after the diagnosis had been established, a tumor was found in the right breast It was a hard, 3 cm mass situated in the lower outer sector of the breast There was retraction of the overlying skin It was excised locally and proved to be metastatic thyroid carcinoma The patient died with cerebral metastases four months after her cough had begun

Subcutaneous Phlebitis of the Breast Region (Mondor's Disease)

An infrequent lesion of the lateral thoracic wall and the breast region, which comes to the attention of those particularly interested in lesions of the breast, is



Fig 263 Subcutaneous phlebitis (Mondor's disease) of the breast region

subcutaneous phlebitis Although good case reports of this disease were published in 1922 by Fiessinger and Mathieu in France, and by Williams and by Daniels in our country a decade later, it is today called Mondor's disease because he described the clinical picture of the disease so well before his fellow Parisian surgeons in 1929 In 1947 Leger collected reports of 22 cases Feldman and his associates have recently published a good description of one more These patients complain of a painful, tender subcutaneous cord which extends either from the region of the anterior axillary fold downward to the lateral aspect of the breast, diagonally across the lateral aspect of the breast, or from the lateral mammary o.

inframammary region diagonally downward toward the epigastric or hypochondrial region The cord stands out sharply when the arm is raised It lies just beneath the skin which is fixed to it When crossing the softer breast tissue it forms a furrow The lesion may be so painful as to cause dyspnea as in Williams case Microscopical studies of the lesion by Hughes and by Lunn and Potter show that it consists of thrombosis of a subcutaneous vein followed by thickening of the vessel wall and a surrounding zone of fibrosis The vein or veins affected are good sized subcutaneous veins which normally cross the lateral chest region and breast from the epigastric or hypochondriac region to the axilla The disease is self limited subsiding after a few weeks Its etiology is unknown It appears to have no relationship to disease in the breast although in one of Lunn and Potter s 5 cases there was a coexisting carcinoma of the breast About half of the reported cases have been in males

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CHAPTER 22

THE PAPILLARY TYPE OF MAMMARY CARCINOMA

Mammary carcinoma which grows in a papillary form within dilated ducts and cysts deserves description as a separate type because it has both clinical and microscopical features which set it apart from other breast carcinomas Very little has been written about the papillary type and the character of the disease is, as a result, not well known This anonymity is due to two facts Papillary carcinoma is infrequent and its microscopical differentiation from benign papilloma has given pathologists much difficulty I will attempt to clarify its microscopical diagnosis and to describe its clinical characteristics

Incidence

Papillary carcinoma is the rarest of several clinical types of mammary carcinoma We have classified only about 1 5 per cent of our Presbyterian Hospital carcinomas as papillary

The ages of our patients with papillary carcinoma averaged 51 years This is only slightly older than the average age for all our patients with breast carcinoma which was 50 years It is definitely older than the average for our Presbyterian Hospital series of patients with benign intraductal papilloma which was 45 years

Clinical Features

Nipple Discharge A nipple discharge occurred in 21 of our 40 patients with papillary carcinoma. In 17 of those who had a discharge it was blood tinged on some occasions at least In the remaining 4 patients, the discharge was serous. These facts about nipple discharge are not very different from those in our series of cases of benign intraductal papilloma except that the frequency of nipple discharge was higher in the latter disease

The nipple discharge was the first sign of the disease in 6 of our 21 patients with papillary carcinoma who had a discharge

Tumor A tumor was present in all 40 of our patients with papillary carcinoma There were several features of the tumors in these patients which distinguished them from the tumors of ordinary mammary carcinomas In 26 of our 40 patients the tumor had a circumscribed or lobular contour in contrast to the more diffuse, poorly delimited, contour of ordinary breast carcinoma. Six of the tumors were cystic Several projected above the skin surface In three patients

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Fig 265 An ulcerated papillary carcinoma of the breast.

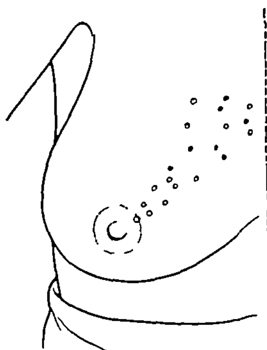


Fig 266 Hard discrete shot like nodules of papillary carcinoma involving a pyramidal area of the upper inner sector of the breast.

the skin over the tumor had a reddish or bluish color Figure 264 shows the redness of the skin over one of these papillary carcinomas In one of the patients the thin bluish skin over the elevated cystic tumor showed several areas of ulceration (Fig 265)

Another type of tumor produced by papillary carcinoma consists of a zone of shotty nodules extending out from the subareolar area toward the periphery of the breast The individual nodules are firm, discrete, movable within the breast, and about 5 mm in diameter Figure 266 reproduces my sketch of the clinical findings in such a papillary carcinoma

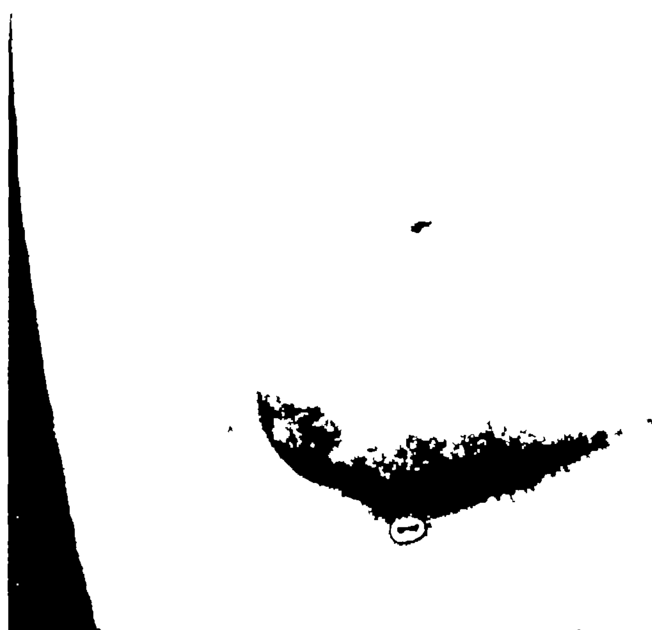


Fig 264 Redness of the skin over a papillary carcinoma of the breast.

In papillary carcinoma the tumor is more likely to be central than in ordinary breast carcinoma In our series of 40 cases, 14 were situated beneath, or adjacent to, the areola This central, as compared to a peripheral, origin suggests that papillary carcinoma has a predilection for the terminal portions of the mammary duct system

Retraction. Retraction signs, either skin dimpling or nipple deviation or retraction, were described in only 18 of our 40 patients with papillary carcinoma In ordinary breast carcinoma retraction is much more frequent The fact that papillary carcinoma grows largely within ducts and cysts no doubt accounts for the lesser degree of fibrosis and retraction that it produces

Duration of Symptoms

The average duration of symptoms in our patients with papillary carcinoma was 12 6 months This can be compared with an average duration of 10 7 months



Fig 265 An ulcerated papillary carcinoma of the breast

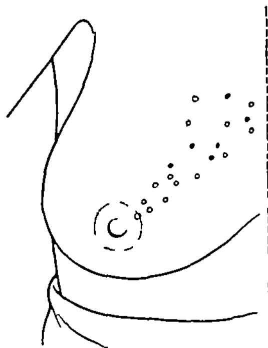


Fig. 266 Hard discrete shot-like nodules of papillary carcinoma involving a pyramidal area of the upper inner sector of the breast.

for ordinary breast carcinoma in the Presbyterian Hospital series of cases The somewhat longer duration of papillary carcinoma is in keeping with its relatively lesser degree of malignancy

Pathology

Surgeon and pathologist can gain important indications of papillary carcinoma from the gross appearance of the lesion When papillary carcinoma grows in a cyst it is soft, friable, and hemorrhagic (Fig 267) When the disease grows in

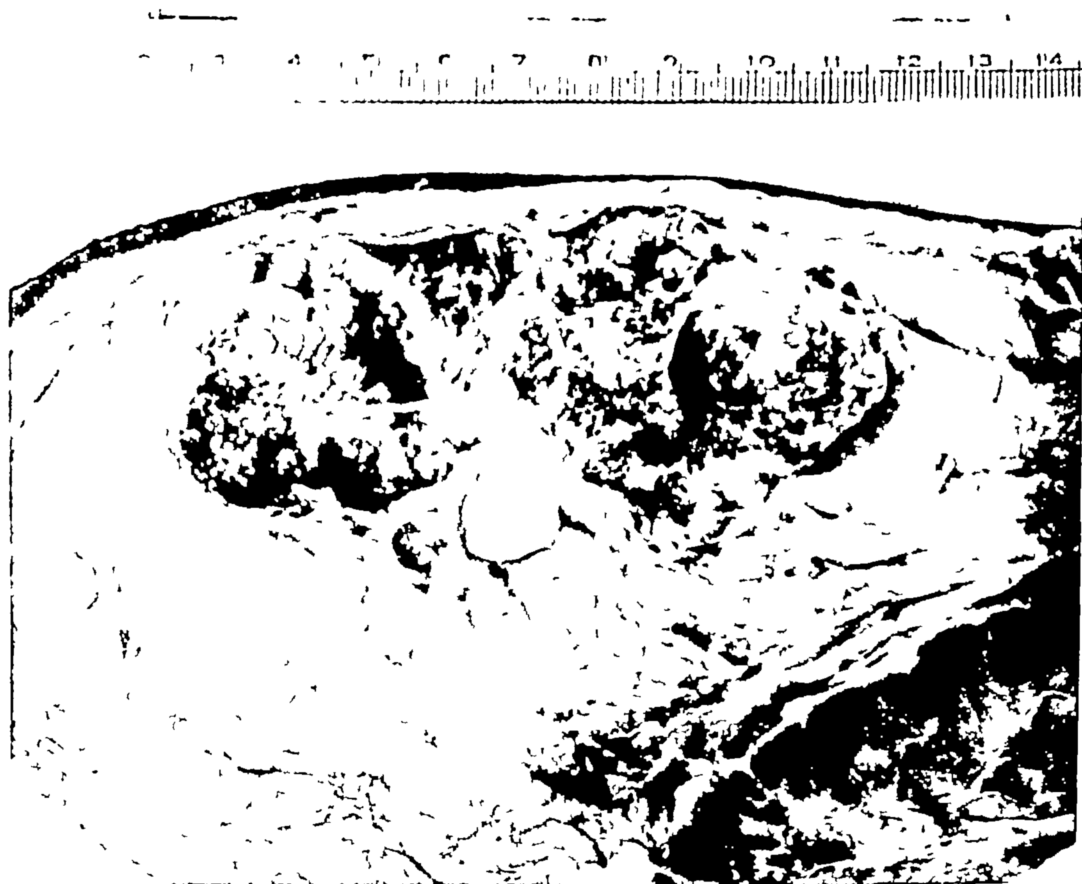


Fig 267 The gross appearance of papillary carcinoma of the breast

dilated ducts they stud the cut surface of the lighter colored breast tissue as circumscribed brownish or reddish nodules

Another gross pathological feature suggesting that a papillary lesion is a carcinoma rather than benign intraductal papilloma is involvement of a wide sector of the breast extending toward its periphery In general, benign papillomas tend to be situated in the main ducts beneath the edge of the areola, or not very far out from it, and to be localized in extent

The ultimate basis for classification of these papillary lesions as carcinomas rather than benign papillomas is, of course, their microscopical structure Both the pattern in which they grow and their cytological atypicalness have a part in the distinction The growth pattern is less important than the cytology For example, among the 40 papillary tumors that we have classified as carcinoma there were a number of very well differentiated lesions in which the growth pattern was indistinguishable from that of benign intraductal papilloma The proliferating cells were supported upon long branching papillary processes with

well developed connective tissue cores Yet these tumors metastasized a fact that can leave no doubt as to their malignant nature

The microscopical criteria that convince us of the malignancy of these lesions include

1 An abnormal degree of variation in the size and shape of the epithelial cells and their nuclei and hyperchromatism of the nuclei Frequent mitoses are an indication of malignancy when seen but a good many of our indubitably malignant papillary tumors did not have them Figure 268 shows an area in a

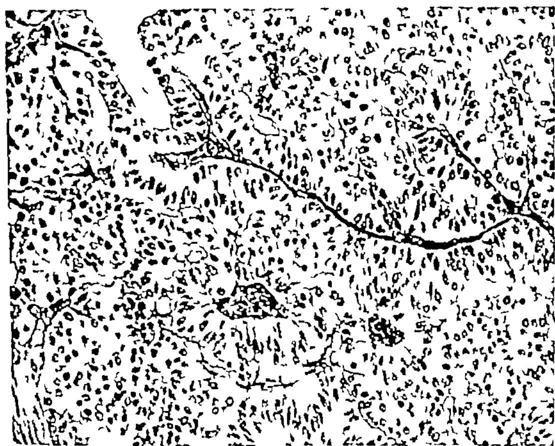


Fig 268 The large hyperchromatic nuclei of the cells of a papillary carcinoma.

papillary tumor where the large hyperchromatic cells and mitoses leave no doubt as to their carcinomatous nature By contrast Figure 269 shows a benign papilloma with its comparatively uniform cells

2 A tendency for the proliferating cells to pile up several layers deep upon the papillary processes with loss of the polarity of the nuclei. Figure 270 shows a papillary carcinoma in which the cells are arranged upon long branching papillary processes with well developed connective tissue cores In a higher power view (Fig 271) the cells are seen to be many layers deep In Figure 272 a metastasis from this tumor to an axillary lymph node is seen to retain in part its papillary character

3 Growth of anaplastic cells in a papillary manner but without supporting connective tissue cores The coreless papillae may be long and branching (Fig 273) or short and blunt (Fig 274)

4 Growth of the cells in broad sheets and masses within the papillary struc

Fig 269 The uniform cells of a benign intraductal papilloma

Fig 270 The long branching papillary processes of a papillary carcinoma

Fig 271 A high power view of a papillary carcinoma showing the cells growing many layers deep on the papillary processes

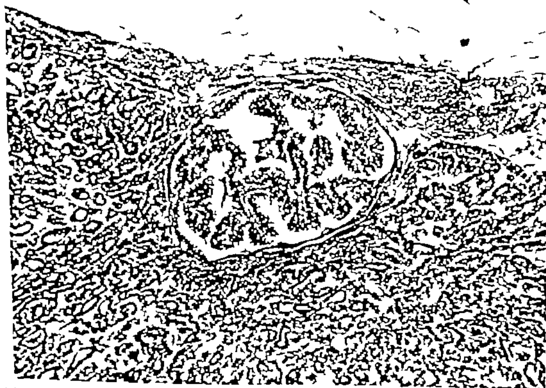


Fig. 272 Metastasis to an axillary lymph node of the papillary carcinoma shown in Figures 270 and 271

Fig 269 The uniform cells of a benign intraductal papilloma

Fig 270 The long branching papillary processes of a papillary carcinoma

Fig 275 The cells of a papillary carcinoma growing in solid masses



Fig. 276 Transformation from a papillary to a solid growth pattern in the wall of a cystic space in a papillary carcinoma

Fig 273 Long coreless papillae of papillary carcinoma

Fig. 274. Short coreless papillae of papillary carcinoma

Fig 278 Axillary lymph node metastasis of papillary carcinoma shown in Figure 277

Fig 279 Papillary carcinoma growing in a solid pattern.

ture, as if the coreless papillary processes had fused Figure 275 shows an area in a papillary carcinoma where the cells are growing in this pattern Figure 276 shows the same process of transformation from a papillary pattern to a solid pattern in the wall of a cystic space in a papillary carcinoma

5 Filling up of the dilated ducts by the fused papillary processes to form a cribriform pattern or solid masses of cells The cribriform pattern is shown in Figure 277 from a papillary tumor that recurred after local excision and metastasized The pattern was maintained in its axillary metastasis (Fig 278) The solid pattern is shown in Figure 279 from a carcinoma growing within ducts both in a solid pattern and in the form of short coreless papillae (Fig 280) It should be emphasized that the finding of one or two ducts filled with cells growing

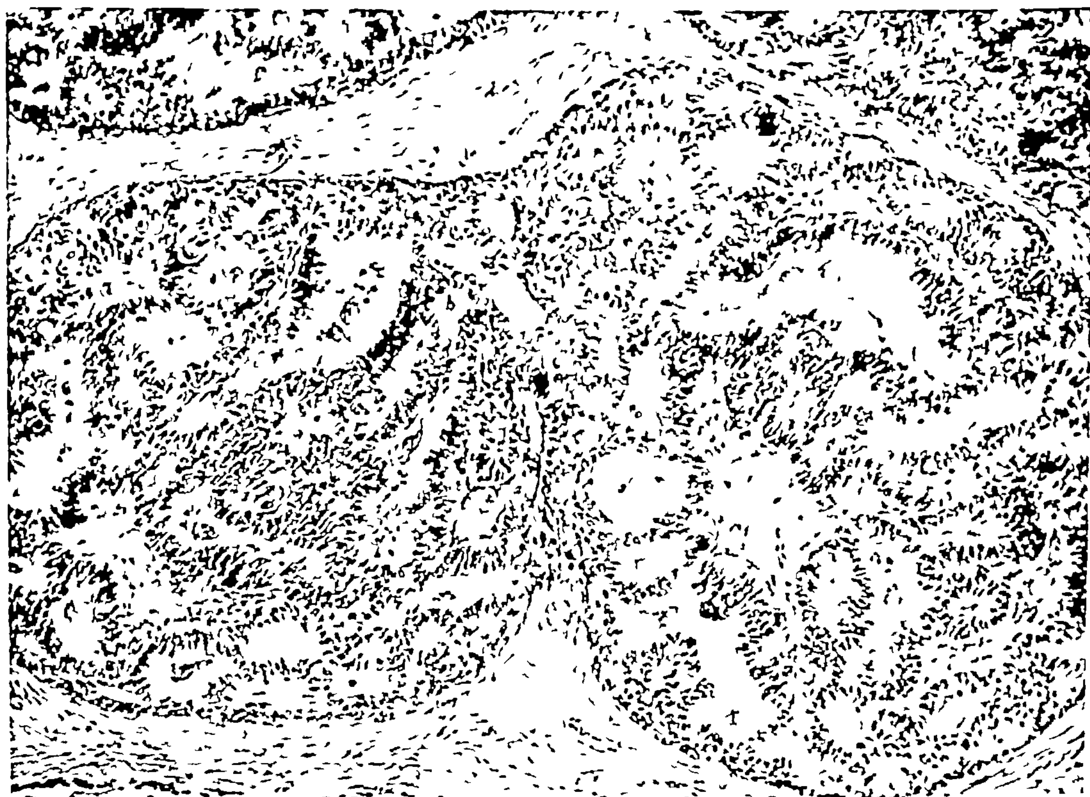


Fig 277 Fused papillae filling up ducts in a cribriform pattern in papillary carcinoma

in these patterns in an area of breast tissue that shows a variety of types of benign epithelial proliferation does not make a diagnosis of carcinoma

6 Invasion of the stroma of the breast is of course an indication of malignancy when it is present, but it was not seen in a number of our well-differentiated, unquestionably malignant papillary lesions If one could study serial microscopical sections from one of these tumors, evidence of invasion would probably be found, but this is impossible We are forced to conclude that invasion, as a histological criterion by itself, is not a prerequisite for diagnosing a papillary lesion as a carcinoma

I have attempted to define the characteristics of the various types of papillary carcinoma in our Presbyterian Hospital series of cases Although their variation in structure is considerable, these tumors all have the common characteristic of growing in a papillary manner within cysts or dilated ducts We have classified

Fig. 278 Axillary lymph node metastasis of papillary carcinoma shown in Figure 277

Fig. 279 Papillary carcinoma growing in a solid pattern.

as papillary only those tumors in which this characteristic predominated We excluded those tumors in which only poorly developed or low papillae were found in scattered ducts, as in many intraductal carcinomas Figure 281 is an example of such an intraductal carcinoma which was *not* classified as papillary.

The final proof that these papillary lesions are malignant is provided by the demonstration of metastasis Axillary lymph node metastases were found in 14 of our 40 cases Seven of these patients with axillary metastases ultimately succumbed to the disease

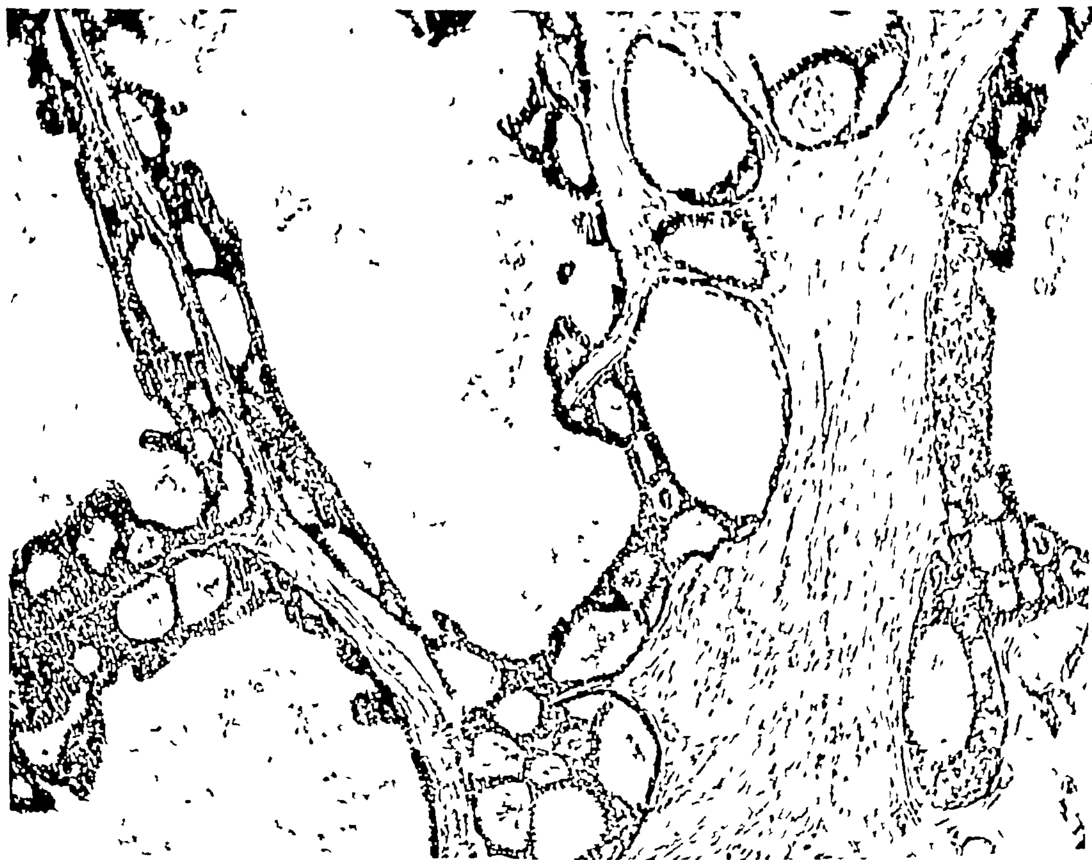


Fig 280 Another area from same papillary carcinoma shown in Figure 279 Here the carcinoma grows as short papillary processes projecting into cystic cavities

As to the question of whether or not these papillary carcinomas have developed from benign intraductal papillomas, I can find no clear evidence of such a relationship either from our Presbyterian Hospital data or from my own experience In our series of 40 papillary carcinomas there were eight in which microscopically benign intraductal papillomas were also found We have even seen typically benign papilloma growing within a dilated duct lined by papillary carcinoma (Fig 282) But it seems to me that the mere association of these two lesions is not proof that the malignant papillary tumors develop from the benign ones We do not conclude that because cysts and carcinomas are often found together, the latter arise from the former We are justified in saying that a woman who has cysts is predisposed to carcinoma because we have established proof of the fact We have no such statistical evidence of a predisposition to papillary carcinoma of women who have had benign intraductal papilloma

Fig. 281 A form of intraductal carcinoma with very low papillary projections which has not been classified as papillary carcinoma

Fig 282. Benign papilloma growing within a dilated duct lined by papillary carcinoma.

To prove that papillary carcinoma evolves from benign intraductal papilloma we would have to be able to document this transformation in a number of case histories Our Presbyterian Hospital series of cases does not include any cases of this kind The first tissue to be studied in every one of our cases showed papillary carcinoma, although in some cases benign papilloma was also found

Differential Diagnosis

A spontaneous serous or bloody nipple discharge at once suggests an intraductal papilloma, but the possibility of carcinoma must always be kept in mind When carcinoma is present it will be found to be the papillary type in the majority of cases In Chapters 20 and 21 I have already discussed the differential diagnosis in patients with a nipple discharge, and emphasized the necessity of surgical exploration

As I warned in discussing the diagnosis of intraductal papilloma in Chapter 13, we have learned not to depend upon frozen sections for distinguishing benign papilloma from papillary carcinoma. When I suspect papillary carcinoma I excise a small representative portion of the lesion, close the wound, and wait for paraffin sections

The risk in thus waiting for a dependable diagnosis is far less of a penalty for the patient than the risk of having her breast removed needlessly Our experience in our Presbyterian Hospital series of cases of papillary carcinoma shows clearly that they are less malignant than ordinary breast carcinoma, and that delay is not such a critical factor

Treatment

Review of the results of treatment in our Presbyterian Hospital series of cases leads us to the conclusion that papillary carcinoma is the least malignant and the most easily cured by surgery of all forms of mammary carcinoma Thirty-two of our patients were treated more than five years ago In 31 of these the breast was eventually removed, although local excision had previously been done unsuccessfully in 4, and irradiation had been tried and had failed in 3 In 29 of the 31 patients the operation was radical mastectomy, and in two simple mastectomy

The five-year results in these 31 patients are shown in Table 83 At least 77 4 per cent appear to have been cured by their operation Five of the 24 patients who were cured by radical mastectomy had axillary metastases

Table 83 Papillary Carcinoma, Five-year Results of Mastectomy in 31 Cases
(Presbyterian Hospital 1915–1950)

	Number	Per cent
Five-year clinical cures	24	77 4
Died in less than 5 years without recurrence	3	9 7
Developed distant metastasis in less than 5 years	3	9 7
Fate unknown	1	3 2
Total	31	100 0

Our data provide good evidence that surgical attack less aggressive than radical mastectomy is inadequate for papillary carcinoma If a simple rather than a radical mastectomy had been done none of these five patients with axillary metastases who were cured would have been saved Local excision of the tumor was first tried in four of our patients and was followed by local recurrence in every case

The comparatively lesser malignancy of papillary carcinoma is indicated by two features of its natural history which are well illustrated in the cases in our series The first of these features is the slow course of the disease This is indicated by the course of the disease in the four patients in whom local excision of the lesion was first performed In these patients an average of 4.2 years elapsed before local recurrence developed and necessitated mastectomy A second remarkable feature of papillary carcinoma is its curability by radical mastectomy even when local excision has been followed by recurrence and axillary metastasis This is rarely possible with ordinary breast carcinoma

The following case illustrates the slow course of the disease as well as its curability by vigorous surgical attack after several unsuccessful attempts at local excision

Mrs. D P a housewife aged 34 discovered a small movable tumor in the upper outer sector of the left breast in October 1943 It was locally excised at a New York hospital and diagnosed microscopically as an intraductal papilloma Eighteen months later local recurrence was noted A second local excision was performed in another New York hospital This time the surgeon removed a great part of the upper outer sector of the breast. Again the lesion was diagnosed microscopically as a papilloma.

One year after the second operation and three and a half years after she had first found a tumor in her breast, a discharge from the nipple developed It was usually serous, but occasionally blood tinged

In January 1947 after another nine months had elapsed, the patient first consulted me I found a firm, poorly delimited tumor measuring 5 x 6 cm. extending from the outer edge of the areola out into the upper outer sector of the left breast. In addition the entire upper half of the breast was studded with small, movable firm nodules lying deep in the breast substance I could not feel any enlarged axillary nodes.

My first step was to biopsy the recurrent tumor in the upper outer sector of the breast. The tissue was studied by frozen sections, and unfortunately we relied upon them, and decided that the lesion was indeed a benign papilloma Because the lesion had recurred twice before, I chose to perform a simple mastectomy including in my dissection the lowest group of axillary lymph glands.

We were distressed to find in study of paraffin sections that the tumor was a well-differentiated papillary carcinoma (Fig. 277) It had involved a great part of the breast. The widely disseminated shotty nodules that had been noted on palpation were all carcinoma, and the disease had extended down through the entire thickness of the breast to involve the pectoral fascia which had been excised with the breast. Metastases were found adjacent to 2 of the 13 axillary lymph nodes (Fig. 278) We were able to secure sections of the lesions removed at the two previous local excisions at other hospitals. It was apparent that the tumor had been a well-differentiated papillary carcinoma from the beginning.

With the diagnosis established I at once performed a radical mastectomy carrying out a specially wide removal of skin and subcutaneous tissues on the chest wall, which required very extensive skin grafting. No additional axillary metastases were found Nine years later the patient continues without any evidence of recurrence

The second case history of papillary carcinoma that I wish to summarize also illustrates the slow course of the disease, which, in this instance, ended fatally

Mrs J R , a nurse, aged 40, was admitted to the Presbyterian Hospital in February, 1938 for treatment of a tumor of her right breast of four months' duration It was situated in the lower inner sector of the breast, measured 5 x 4 cm , and was well delimited and movable It was excised locally and mistakenly diagnosed as a benign intraductal papilloma We today recognize the lesion as a well-differentiated papillary carcinoma

Three and a half years later, in September, 1941, she was again admitted to the hospital for a recurrence measuring 4 x 2 cm at the site of the original tumor Biopsy now led to the correct diagnosis of papillary carcinoma, and radical mastectomy was performed The tumor was found to involve the breast very extensively, and there was a metastasis in one of the 20 lymph nodes removed in the axillary dissection

In February, 1952, ten and one half years after her radical mastectomy, enlargement of right supraclavicular and lower cervical nodes was noted, and a neck dissection revealed metastases from her breast carcinoma She developed pulmonary metastases, and died in October, 1954, sixteen and a half years after the onset of her papillary carcinoma

Radiotherapy has not been a successful method of treatment in the three patients in our series of cases of papillary carcinoma in which it was given as the primary treatment It failed to control the local tumor, except temporarily, in all three One patient died within a year with liver metastases, and the other two, whose tumors recurred locally one year and four years, respectively, after irradiation, were then treated by radical mastectomy and apparently cured

Reference

Stewart, F W Tumors of the Breast Atlas of Tumor Pathology, Section IX, Fascicle 34 Washington, D C , Armed Forces Institute of Pathology, 1950

CHAPTER 23

PAGET'S CARCINOMA OF THE BREAST

More than a hundred years have gone by since Velpeau first described the lesion of the nipple that is today generally called Paget s disease in the following words

"In two such cases the crusts covering the nipple were thick, cracked and adherent, and gave exit to a bloody discharge when an attempt was made to detach them In one of the patients they were of a greenish and in the other of a yellowish grey color

"In these as in many other instances the disease had lasted for several years and was accompanied by itching but without any marked inflammatory symptoms Underneath the crusts there was neither fissure nor destruction of tissue but simple excoriation Everything indicated that the epidermis alone had under gone destruction and that the free surfaces of the lobules and little glands of the organ were the seat of the disease The nipple looked like a raspberry or straw berry and rather suggested the idea of the granular neck of the uterus

Velpeau could not have followed his patients, for he was unaware of any relationship of this nipple lesion to carcinoma It was James Paget, in 1874 who first observed that the nipple erosion was associated with breast cancer His terse clinical description of the disease, which follows could scarcely be improved upon—

'The patients were all women various in age from 40 to 60 or more years having in common nothing remarkable but their disease In all of them the dis ease began as an eruption on the nipple and areola In the majority it had the appearance of a florid, intensely red raw surface very finely granular as if nearly the whole thickness of the epidermis were removed like the surface of very acute diffuse eczema, or like that of an acute balanitis From such a surface, on the whole or greater part of the nipple and areola, there was always copious clear yellowish viscid exudation The sensations were commonly tingling, itching, and burning, but the malady was never attended by disturbance of the general health. I have not seen this form of eruption extend beyond the areola, and only once have seen it pass into a deeper ulceration of the skin after the manner of a rodent ulcer

In some of the cases the eruption has presented the characters of an ordinary chronic eczema, with minute vesications, succeeded by soft, moist, yellowish scabs or scales and constant viscid exudation In some it has been like psoriasis dry with a few white scales slowly desquamating and in both these forms

The second case history of papillary carcinoma that I wish to summarize also illustrates the slow course of the disease, which, in this instance, ended fatally

Mrs J R , a nurse, aged 40, was admitted to the Presbyterian Hospital in February, 1938 for treatment of a tumor of her right breast of four months' duration It was situated in the lower inner sector of the breast, measured 5 x 4 cm , and was well delimited and movable It was excised locally and mistakenly diagnosed as a benign intraductal papilloma We today recognize the lesion as a well-differentiated papillary carcinoma

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Reference

Stewart, F W Tumors of the Breast Atlas of Tumor Pathology, Section IX, Fascicle 34 Washington, D C , Armed Forces Institute of Pathology, 1950

cells are at first scattered and isolated but as the invasion progresses they are seen in groups and masses In good microscopical sections in which the cytologi cal details are well shown these Paget cells are obviously malignant in nature. They have the large irregular hyperchromatic nuclei of carcinoma cells Al though Paget s cells often have the characteristic large, clear cytoplasms, this feature is not a constant one In some specimens the cells have the usual appear ance of duct carcinoma cells which of course they are They may even form acini, as shown in Figure 284

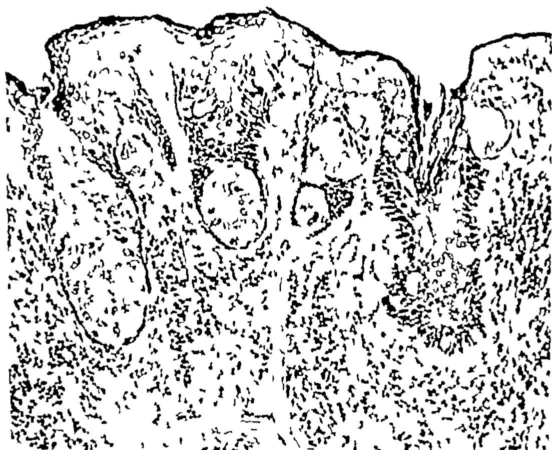


Fig 283 Paget s cells infiltrating the epidermis of the nipple

Their origin from intraductal carcinoma in the nipple ducts can be traced in specimens which are properly studied microscopically Figure 285 shows a vertical section through a nipple in which the intraductal carcinoma extends upward *along the duct wall to the level of the nipple epidermis.* From this point the carcinoma cells have grown out into the nipple epidermis and appear as Paget cells In this case this was the only nipple duct in which carcinoma was found, although there was extensive carcinoma in the breast itself Usually a number of the nipple ducts are involved by the carcinoma. In a recent patient of mine in whom the nipple erosion had been present for seven months but no breast tumor was palpable a transverse section through the base of the nipple (Fig 286) showed that *20 of 21 nipple ducts were involved* In these ducts the disease is seen in higher magnification (Fig 287) to consist not of a solid column of carcinoma cells filling the duct lumen but of a cylinder of carcinoma cells

especially in the psoriasis, I have seen the eruption spreading far beyond the areola in widening circles, or, with scattered blotches of redness, covering nearly the whole breast

"I am not aware that in any of the cases which I have seen the eruption was different from what may be described as long-persistent eczema, or psoriasis, or by some other name, in treatises on diseases of the skin, and I believe that such cases sometimes occur on the breast, and after many months' duration are cured, or pass by, and are not followed by any other disease But it has happened that in every case which I have been able to watch, cancer of the mammary gland has followed within at the most two years, and usually within one year The eruption has resisted all the treatment, both local and general, that has been used, and has continued even after the affected part of the skin has been involved in the cancerous disease

"The formation of cancer has not in any case taken place first in the diseased part of the skin It has always been in the substance of the mammary gland, beneath or not far from the diseased skin, and always with a clear interval of apparently healthy tissue

"In the cancers themselves, I have seen in these cases nothing peculiar They have been various in form, some acute, some chronic, the majority following an average course, and all tending to the same end, recurring if removed, affecting lymph-glands and distant parts, showing nothing which might not be written in the ordinary history of cancer of the breast

"The single noteworthy fact found in all these cases is that which I have stated in the first sentence, and I think it deserves careful study For the sequence of cancer after the chronic skin-disease is so frequent that it may be suspected of being a consequence and must be always feared, and may be sometimes almost certainly foretold "

Pathology

In discussing Paget's carcinoma it is desirable to deal first with the pathology of the disease, because its natural history and clinical classification can be understood only in the light of our knowledge of the pathological process

The first step in this direction was the microscopical recognition of the large cells with pale cytoplasms and prominent irregular nuclei, occasionally seen in mitoses, occurring singly or in clumps in the nipple epidermis, which we now call Paget's cells Darier first described these cells in 1889 but mistakenly regarded them merely as degenerated epidermal cells There has since been much controversy regarding the nature of the cells but the fact is now established beyond any reasonable doubt that they are carcinoma cells that have invaded the epidermis of the nipple from carcinoma in the subjacent nipple ducts It was Jacobaeus who, in 1904, first traced their origin from intraductal carcinoma in the nipple ducts These Paget cells have a peculiar and special facility for invading epithelium—in the epidermis of the nipple as well as in the epithelial lining of the mammary ducts This invasive process has been well described during recent years by Simard, by Inglis, and by Muir

The appearance of Paget's cells as they infiltrate the epidermis of the nipple, producing an erosion evident clinically, is shown in Figure 283 The Paget

with Paget s carcinoma treated by radical mastectomy 47 8 per cent had axillary metastases



Fig 285 Intraductal carcinoma growing along a nipple duct up to the level of the epidermis in Paget s carcinoma

Figure 288 shows in low power a vertical section of a breast in which Paget s cells are seen in the nipple epidermis (A) while in the depths of the breast there is a small infiltrating carcinoma (C) The two lesions are seen to be connected by a duct lined by intraductal carcinoma (B) Figure 289 shows in higher power the

that has replaced the normal two layer columnar epithelium of the duct Each involved duct is seen to be surrounded by a collar of lymphocytes When so many ducts are involved by the carcinomatous process it would seem that it must have had a multicentric origin

Both Muir and Inglis have published superb photographs of this form of intraductal carcinoma in the nipple ducts and its extension upwards into the



Fig 284 Paget's cells forming acini as they infiltrate the nipple epidermis

nipple epidermis Both of these students of Paget's carcinoma agree that the intraductal carcinoma is the basic lesion of the disease They differ in their interpretation of the fact that in most cases of Paget's carcinoma, intraductal carcinoma is found not only in the nipple ducts but also somewhere in the ducts in the breast The deeper intraductal carcinomas are fully malignant They break through the duct walls, assume the character of a variety of types of breast carcinoma, and metastasize In our Presbyterian Hospital series of 69 patients

with Paget s carcinoma treated by radical mastectomy 47 8 per cent had axillary metastases



Fig 285 Intraductal carcinoma growing along a nipple duct up to the level of the epi dermis in Paget s carcinoma.

Figure 288 shows in low power a vertical section of a breast in which Paget s cells are seen in the nipple epidermis (A) while in the depths of the breast there is a small infiltrating carcinoma (C) The two lesions are seen to be connected by a duct lined by intraductal carcinoma (B) Figure 289 shows in higher power the

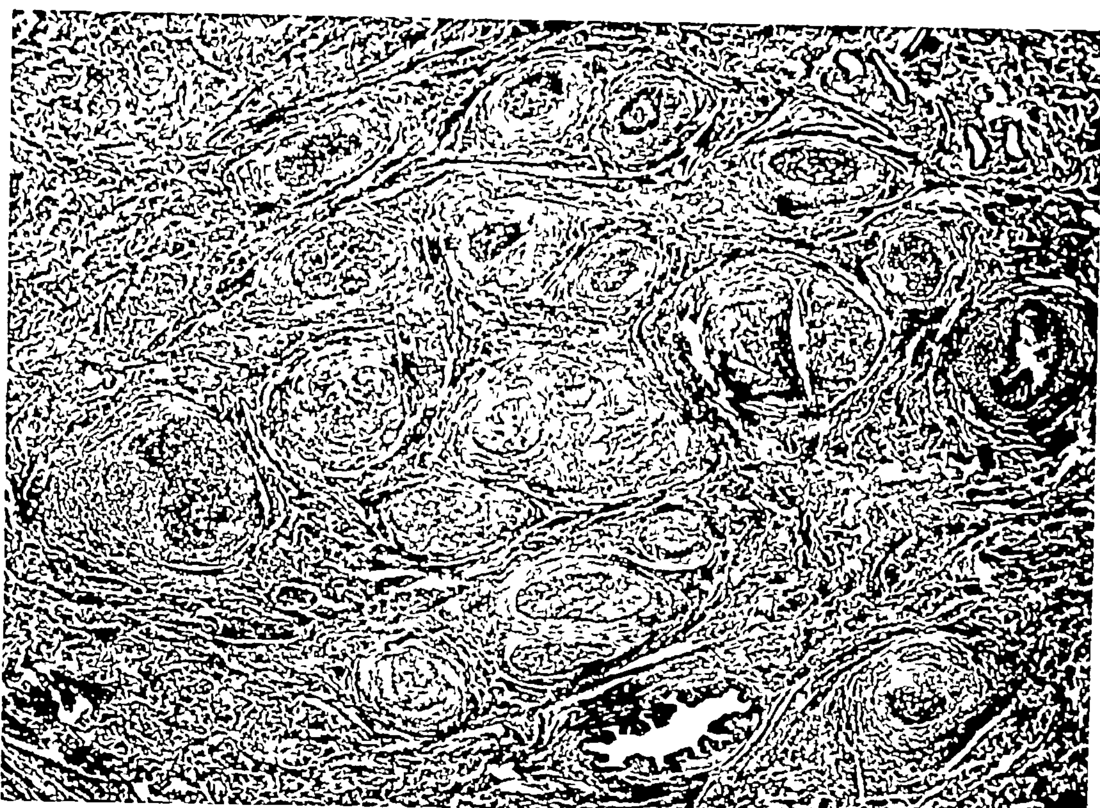


Fig 286 Transverse section through nipple in Paget's carcinoma, showing 20 of 21 nipple ducts involved by the disease

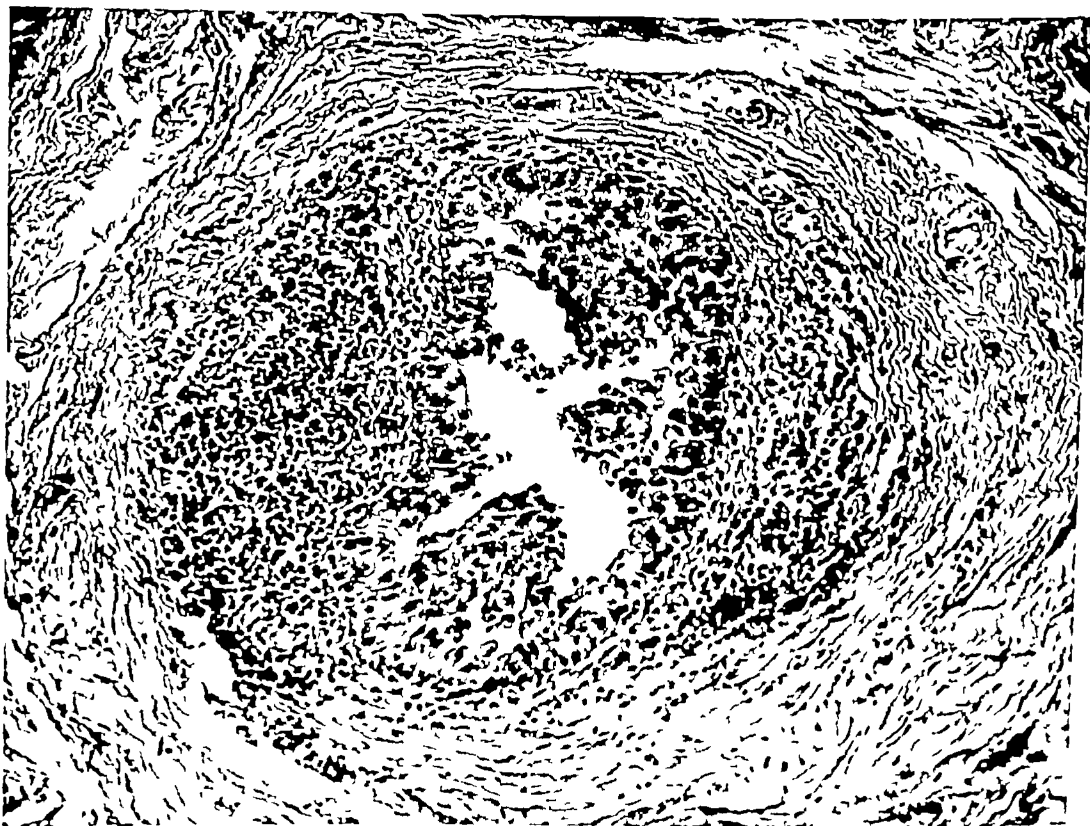


Fig 287 Nipple duct involved by Paget's carcinoma—higher power of Figure 286

carcinoma deep in the breast and Figure 290 the carcinoma in the connecting duct The Paget cells in the nipple epidermis are seen in Figure 283

Inglis believes that the intraductal carcinoma of this disease is a special form of duct carcinoma that originates in the nipple ducts and spreads downward by continuity in the epithelium of the duct system and produces the carcinoma so



Fig 288 Low power vertical section through breast containing Paget s carcinoma. *A* Paget s cells in epidermis *B* duct lined by intraductal carcinoma. *C* infiltrating carcinoma in depths of the breast

frequently found in the depths of the breast Muir on the other hand believes that the intraductal carcinoma of Paget s carcinoma is fundamentally no different from other breast duct carcinomas It may originate in any part of the duct system and may arise in multiple independent foci If it develops first in the ducts of the nipple it may spread to the nipple epidermis and produce Paget s erosion More commonly it develops in the ducts in the breast proper and breaks through

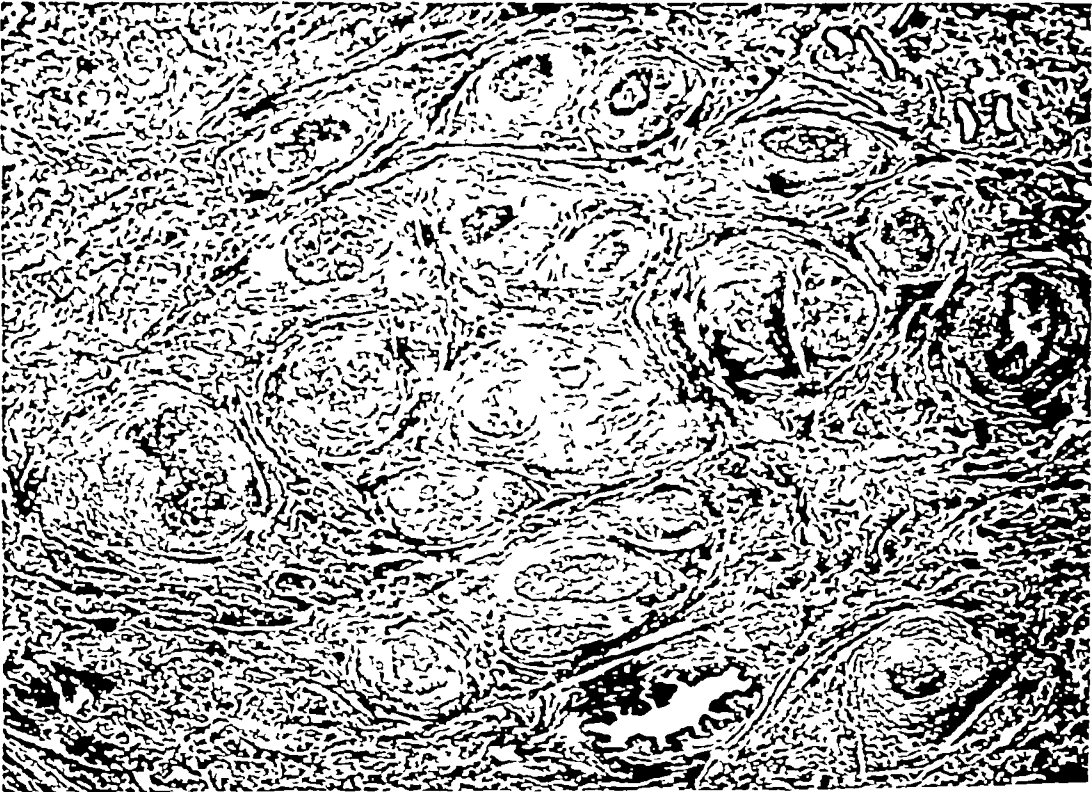


Fig 286 Transverse section through nipple in Paget s carcinoma, showing 20 of 21 nipple ducts involved by the disease

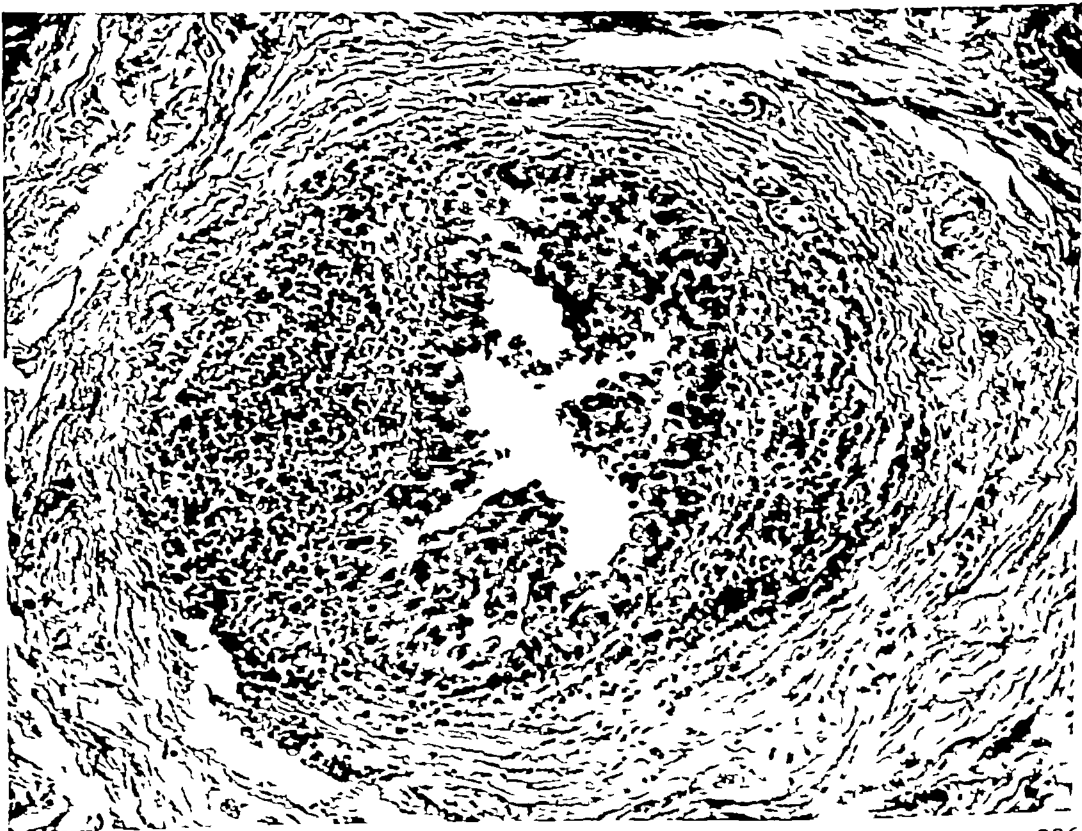


Fig 287 Nipple duct involved by Paget s carcinoma—higher power of Figure 286

But Inglis carries this concept too far when he argues that the carcinoma in the depths of the breast is the result of infiltration of the nipple duct carcinoma down wards in the epithelium of the duct system We have numerous cases in our series in which there is very extensive carcinoma in the breast but minimal nipple duct carcinoma in these cases the breast carcinoma almost certainly developed first

These questions of where the intraductal carcinoma of Paget s disease origi nates, and how it spreads, cannot be answered definitively as yet because ade quate microscopical evidence is not available In the first place, the disease is infrequent and the number of cases available for study small The best case series studied microscopically have been Cheatle s (17 cases) Inglis (24 cases) and Muir s (40 cases) Cheatle devoted one-sixth of his book Tumors of the Breast to presenting the details of his study by the whole breast section method of his 17 cases of Paget s disease This great effort did not solve the problem because the cytology in whole breast sections is not the best and because the sections were unfortunately cut vertically It is obvious that the only method by which the relationship of lesions in the nipple and nipple ducts to lesions in the underlying breast ducts and in the breast as a whole can be accurately determined is by horizontal serial key block sections No pathologist has yet carried out this great labor in a significantly large series of cases

Lacking such information all that we can do is to use what data we do have to classify the reported cases of Paget s disease into two groups, as follows

1 Those in which intraductal carcinoma is found only in the nipple ducts, from which its cells have invaded the nipple epidermis as Paget cells

2. Those in which there is not only intraductal carcinoma in the nipple ducts, but also in deeper ducts in the breast itself

Table 84 presents Cheatle s and Muir s cases as well as our own from the Presbyterian Hospital classified in this manner

Table 84. Classification of Paget's Carcinoma According to Site of Involvement

Site of involvement	Cheatle	Muir	Presbyterian Hospital
Intraductal carcinoma, nipple only	3	5	5
Intraductal carcinoma in nipple and also in breast	14	34	77
Total	17	39	82

In occasional mammary carcinomas of no special type the carcinoma extends upwards until it reaches the nipple and areolar region and finally invades the epidermis This kind of contact invasion of the nipple epidermis can result in erosion but it should not be confused with the type of erosion described by Paget The two types of erosion are different clinically In that due to contact invasion of the nipple by ordinary breast carcinoma the nipple is usually retracted, and fixed to the underlying carcinoma. In the erosion of Paget s carcinoma the nipple continues to be erect and movable for a long time It is destroyed only after the erosion involves the whole of the nipple epidermis and extends out into the areola and the skin over the breast.

Fig 289 Higher power of the carcinoma in the depths of the breast shown in Figure 288



Fig 290 Higher power of the intraductal carcinoma in the duct leading up to the nipple shown in Figure 288

the duct walls to become infiltrating breast carcinoma To Muir the Paget type of carcinoma is therefore merely "a rare complication of a quite common condition," i e , intraductal carcinoma

The clinical fact which was emphasized by Paget himself, namely, that the nipple erosion usually precedes the tumor in the breast, might be said to favor Inglis' concept that the intraductal carcinoma develops first in the nipple ducts

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Study of the pathology of Paget's disease in our series of 90 cases leads us to a point of view similar to Muir's The basic lesion is intraductal carcinoma, usually multicentric not only in the duct system of the breast but also in the nipple ducts Although the intraductal carcinoma is usually well-differentiated, we must assume that it is fully malignant It penetrates the duct walls and invades the breast, and metastasizes, even though we do not always happen to see its invasive phase in the minute portion of the lesion shown in the microscopical sections available in the individual case The intraductal carcinomas of Paget's disease are of varied morphology Figures 291, 292, 293, and 294 show some of the types that we found in our series of cases

The microscopical feature that distinguishes the intraductal carcinoma of the disease described by Paget from other intraductal breast carcinomas is its situa-



Fig 291 A type of intraductal carcinoma in the breast itself in Paget's carcinoma

tion in the terminal portion of the nipple ducts and its infiltration of the nipple epidermis Without these features no lesion can be classified as Paget's carcinoma The epidermal infiltration by Paget's cells need not, however, have reached the stage of producing an erosion It is sufficient that on microscopical examination only a few Paget's cells are seen in the epidermis In 21 of our 90 cases there was no clinically evident nipple erosion

Our cases showed a wide range in the extent of the intraductal carcinoma in the nipple ducts and in the breast In the 82 cases in our Presbyterian Hospital series available for study regarding this point, there were 5 in which there was no carcinoma in the breast itself, the disease being found only in the nipple ducts In approximately 15 of the remaining cases, only one focus of carcinoma was found in the breast, in addition to that identified in the nipple ducts In all the other cases there were multiple foci of carcinoma in the breast In many of the

Fig. 292. Another type of intraductal carcinoma in the breast in Paget's carcinoma

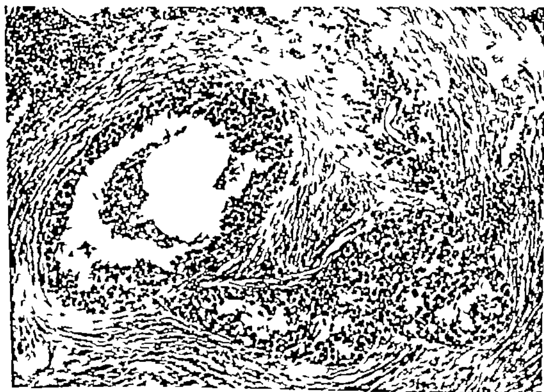


Fig. 293 Another type of intraductal carcinoma in the breast in Paget's carcinoma

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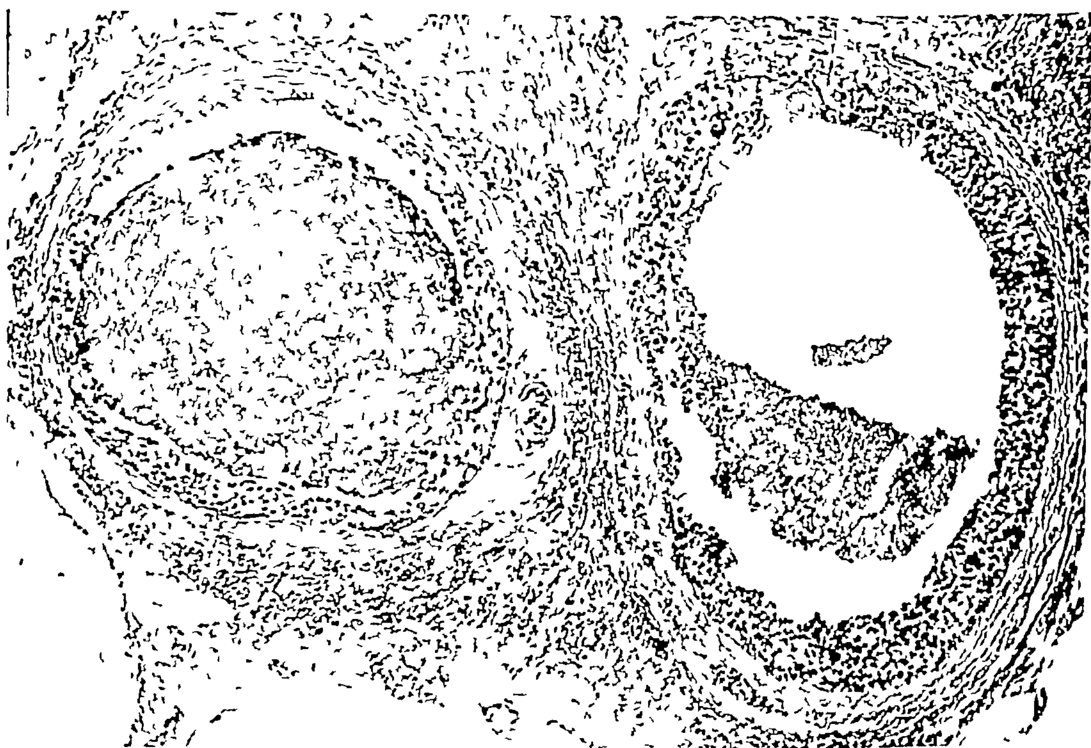


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Mrs. K G a housewife aged 43 found a lump in her right breast and came to her surgeon in the Presbyterian Hospital a month later She had had no symptoms referable to the nipple.

Examination showed a 5 x 6 cm firm mass in the upper outer sector of the right breast. The mass was movable and there was no skin retraction. There was a single, firm 1.5 cm right axillary node. A firm, 1 5 cm tumor was also found in the lower outer sector of the left breast. Both nipples appeared to be normal

The right-sided breast tumor was biopsied and shown to be a carcinoma. Radical mastectomy was done Pathological study showed two carcinomas in this breast, a very large one in the upper outer sector and a small one in the lower inner sector Both were

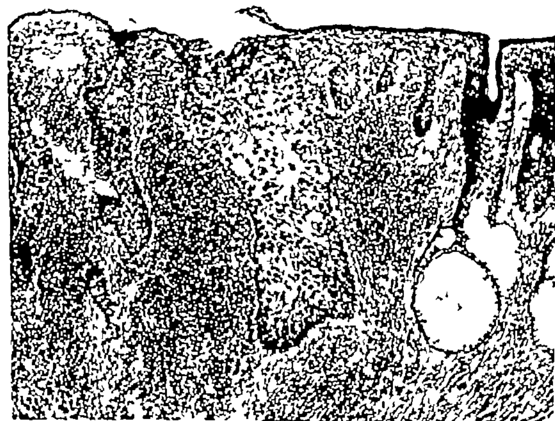


Fig 295 Intraductal carcinoma in a single nipple duct, and Paget s cells in the nipple epithelium, as the only evidence of Paget s carcinoma

of the intraductal type Sections through the nipple showed intraductal carcinoma in a single nipple duct near its termination, and Paget s cells in the adjacent nipple epidermis Figure 296 shows the involved duct.

Two weeks after the right radical mastectomy the tumor in the left breast was biopsied It was proved to be a carcinoma. Simple mastectomy was done Pathological study showed an intraductal carcinoma that was regarded as being of independent origin from the right sided carcinoma

This case is an example of far advanced, extensive and probably long standing, bilateral intraductal breast carcinoma in which there was in one nipple a minimal degree of involvement of one nipple duct, with Paget cells in the adjacent nipple epidermis

cases there was intraductal carcinoma in widely dispersed ducts in the breast The multiplicity and extent of the intraductal carcinoma in the breast in our cases makes it impossible for us to accept Inglis' concept that the duct system of the breast is involved by downward growth of the intraductal carcinoma in the nipple ducts We prefer Muir's point of view that the intraductal carcinoma usually originates in multiple foci both in the nipple ducts and in the ducts of the breast itself

To illustrate the variation in the extent of the intraductal carcinoma in Paget's disease, I will summarize two cases



Fig 294 Another type of intraductal carcinoma in the breast in Paget's carcinoma.

Miss C T, an unmarried office worker aged 43, came to my associate, Dr David Habif, complaining of "eczema" of the nipple which she had had for two years When it first developed she consulted her physician, who gave her Aureomycin ointment It healed temporarily but soon broke open again Tar ointment had made it worse

The nipple was erect, and normal in shape The epithelium of the entire surface of the nipple was eroded, and appeared bright red and granular The erosion also extended out onto the areola at one point There was no tumor palpable in the breast A 1 cm firm axillary node was felt in the axilla

Biopsy of the nipple erosion performed in the office with Novocain showed typical Paget's carcinoma Radical mastectomy was then carried out

The microscopical studies showed intraductal carcinoma in the terminal portion of a single nipple duct (Fig 295) from which Paget cells infiltrated the nipple epithelium extensively and produced a large erosion More than 100 sections from the breast failed to show any carcinoma in it There were no metastases in 49 lymph nodes

This case, then, is an example of an early stage of the disease, the intraductal carcinoma being found only in a single nipple duct

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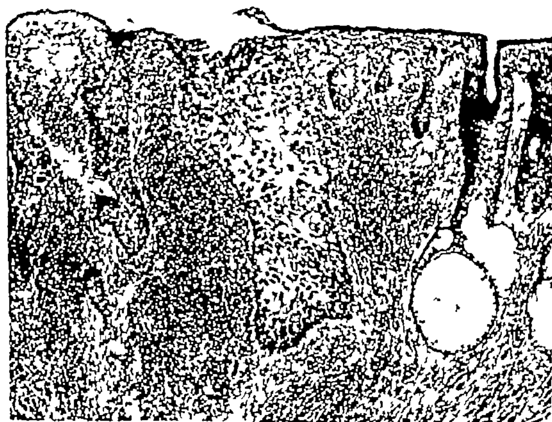


Fig. 295 Intraductal carcinoma in a single nipple duct and Paget s cells in the nipple epithelium as the only evidence of Paget s carcinoma.

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This case is an example of far advanced, extensive and probably long standing, bilateral intraductal breast carcinoma, in which there was in one nipple a minimal degree of involvement of one nipple duct, with Paget cells in the adjacent nipple epidermis

Incidence

Paget's carcinoma is uncommon In our data it has constituted about 3 per cent of all mammary carcinomas A few examples of Paget's carcinoma have been reported in males (Sarason and Prior, Treves) All our cases have occurred in females

The mean age of our patients with Paget's carcinoma has been 50 years, approximately the same as in our series of breast carcinomas as a whole



Fig 296 A single nipple duct involved by carcinoma in an advanced breast carcinoma

Symptoms

The first symptom of Paget's carcinoma is often itching, or burning or smarting of the nipple It was noted in the histories of 36 per cent of our patients who had a nipple erosion A frequent story is that the patient next finds a brownish spot on her brassiere or nightgown, and on inspecting her nipple she discovers a small yellowish-gray, crusted area, or a tiny bright red erosion Figure 297 shows such an erosion The erosion often crusts over after being cleaned and treated with ointment of some kind But after a few days or weeks it inevitably breaks open again The enlargement of the erosion is so slow, however, that many months may go by before much of the nipple surface is involved It is difficult for the patient or her physician to believe that such a small and seemingly innocuous lesion can be a cancer

The nipple erosion is not always circular It may take the form of a transverse crevice in the nipple When the edges of the crevice are pulled apart its base has the characteristic bright red granulomatous appearance

When the Paget cells have infiltrated the whole of the nipple epidermis they involve the areolar epidermis Figure 298 shows such an erosion extending onto the areola Extension into the skin of the breast occurs next Figure 299 shows a patient of mine whose Paget s erosion had been present for seven years and involved most of the skin over the breast. Radical mastectomy with a large skin graft was done. There were no involved axillary nodes She is well today fifteen years after her operation

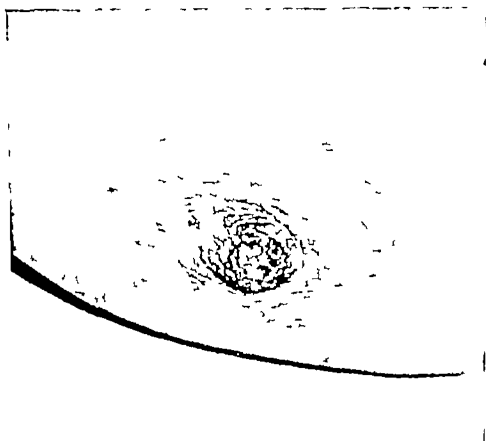


Fig 297 A small nipple erosion in Paget s carcinoma of the breast.

In a considerable proportion of patients with Paget s erosion of the nipple, careful palpation of the breast will reveal a tumor with the clinical characteristics of carcinoma. In our Presbyterian Hospital series of 90 patients with Paget s carcinoma 75 5 per cent had an erosion of the nipple and 58 5 per cent of these patients with a nipple erosion had a palpable breast tumor

There is a third group of patients with breast carcinoma evidenced by a tumor who have no visible gross abnormality of the nipple, but in whom careful microscopical study of the nipple reveals carcinoma in its ducts and Paget s cells infiltrating the epidermis Dockerty and Harrington have called this "preclinical"



Fig 298 Paget's erosion of the nipple extending onto the areola

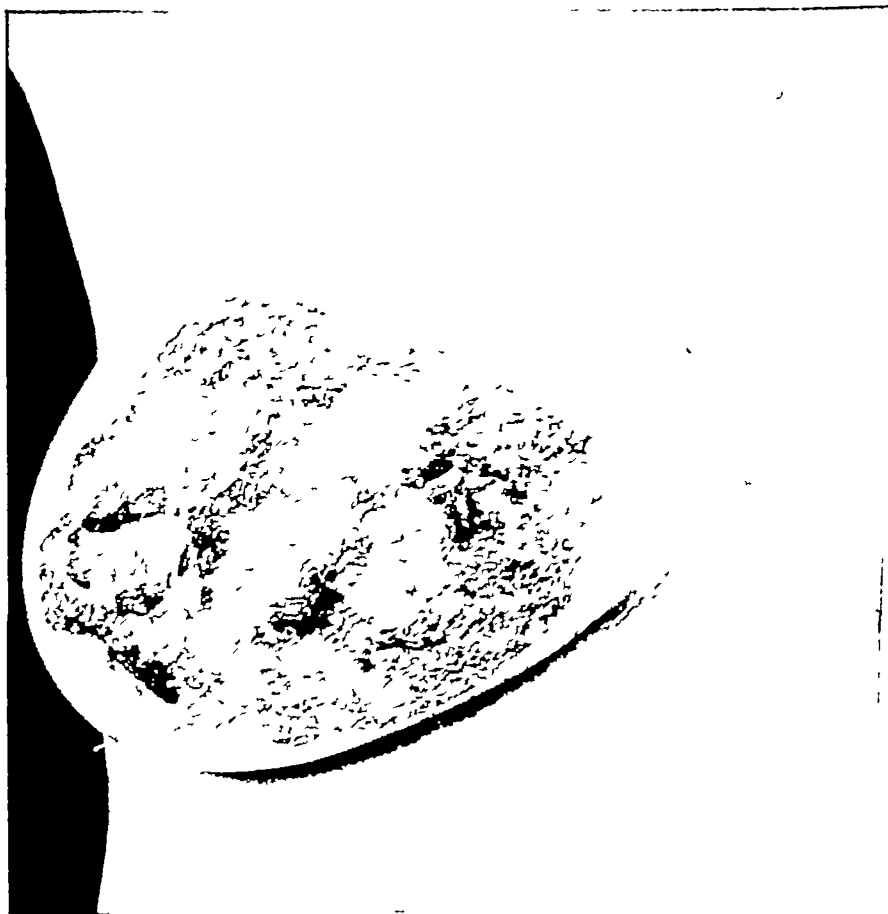


Fig 299 Extensive Paget's erosion, involving most of the skin over the breast, of 7 years' duration

Paget s disease in a paper in which they describe seven such cases There were 22 such cases in our Presbyterian Hospital series

Clinical Classification of Cases

On the basis of these clinical features there are three types of Paget s carcinoma

1 The patients in whom the nipple symptoms—itching and erosion—are the only manifestations of the disease

2. The patients in whom there is not only a nipple erosion but in addition a breast tumor

3 The patients with a breast tumor but no clinical sign of a nipple lesion in whom microscopical study nevertheless shows carcinoma in the nipple ducts and Paget cells in the nipple epidermis

Table 85 shows our Presbyterian Hospital cases of Paget s carcinoma classified in these three groups

Table 85. Clinical Classification of 90 Cases of Paget s Disease
(Presbyterian Hospital 1915–1955)

Clinical signs	Number of cases	Percentage of total number of cases
1 Nipple erosion only	28	31 1
2. Nipple erosion and breast tumor	40	44 4
3 Breast tumor only	22	24 4
Total	90	

Diagnosis

Paget s carcinoma is the easiest form of breast carcinoma to detect because the nipple lesion frequently produces itching or burning which calls the patient s and the physician s attention to it, and because it often takes the form of obvious crusting and erosion of the nipple Unlike ordinary breast carcinoma the Paget type is neither silent nor invisible Nevertheless the diagnosis is missed more often, and treatment delayed longer than in ordinary breast carcinoma The data regarding delay and diagnostic failure in our series of cases of Paget s carcinoma are shown in Table 86 It will be seen that the average delay was 15.2 months This is more than twice as long as the average delay in my personal series of patients with ordinary breast carcinoma The frequency with which the diagnosis was missed by physicians was twice as high for Paget s carcinoma as for ordinary carcinoma, and the additional delay chargeable to physicians in those patients in whom they missed the diagnosis was about five months longer in Paget s carcinoma.

The fundamental reason for this bad diagnostic record is I believe, the simple fact that it is difficult for both patients and physicians alike to realize that such a seemingly innocuous minute lesion on the surface of the nipple can be a manifestation of a vicious carcinoma This is excusable on the part of the patient, but on the part of the physician who fails to recognize the disease it is a sad reflection upon the inadequacy of our methods of medical education. These

patients are often sent from one physician to another, frequently to dermatologists, and all sorts of misguided therapy—salves, cauterization, irradiation—are given without the true nature of the nipple erosion being discovered In our own department of dermatology the diagnosis has often been missed It is, of course, true that surgeons also sometimes fail to diagnose Paget's carcinoma, but in my experience dermatologists have been guilty more often than any other group of specialists

The following case history is so typical that I think it worth summarizing

Mrs K S , a graduate nurse aged 54, felt a sudden momentary stinging pain in her left nipple After this episode the nipple began to itch, and two weeks later she first noted a small erosion on the surface of the nipple She went to her family physician who told her that he was puzzled by the lesion He gave her an ointment to apply The erosion healed over partially but broke open again after a few weeks Her physician then sent her to a radiotherapist who irradiated the nipple twice a week over a period of six months The erosion still persisting, her physician sent her to me

Table 86. Delay in Patients with Paget's Carcinoma
(Presbyterian Hospital, 1915–1955)

Type	Number of cases	Average duration of symptoms (months)	Diagnosis missed by physicians		Average additional delay due to physician failure (months)
			Number	Per cent	
Nipple erosion only	28	16 2	16	57 1	16 5
Nipple erosion and breast tumor	40	15 4	20	50 0	15 6
Breast tumor only	22	13 4	7	31 8	26 6
Total	90	15 2	43	47 8	17 9
Personal series of cases Breast carcinoma (all types) 1943–54	546	7 5	115	21 1	12 5

I saw her for the first time seven months after her initial symptom The surface of the nipple showed a moist, bright red, granular erosion, measuring 1 cm in diameter The breast was otherwise normal No tumor was palpable There were no enlarged axillary or supraclavicular lymph nodes

A 5 mm wedge of the erosion was excised under Novocain anesthesia It showed Paget's carcinoma in the epidermis There was some squamous metaplasia of the carcinoma cells which was interpreted as the result of the irradiation

Radical mastectomy was performed Intraductal carcinoma was found in 20 of 21 nipple ducts, but nowhere else in the breast There were no metastases in 31 axillary lymph nodes

Paget's carcinoma is most often mistaken for dermatitis of the nipple and areola It is true that dermatitis, sometimes of the contact type due to irritation from clothes or cosmetics, sometimes due to bacterial infection, sometimes of

unknown etiology develops in the nipple and areola But dermatitis is so much less frequent than Paget s carcinoma that every lesion of the nipple and areolar epithelium should be assumed to be carcinomatous until proven otherwise

A rule that suggests itself to me is that all erosions and dermatitis-like lesions that involve the nipple epithelium *only* are carcinomatous I have not seen one that was not. Lesions that involve the areolar as well as the nipple epithelium and sometimes the skin of the breast are usually carcinomatous, but occasionally they are due to dermatitis Erosions that involve the areola or the skin of the adjacent breast, leaving the nipple uninvolved are not Paget s carcinoma Figure 300 shows such an area of dermatitis involving only the areola

Benign dermatitis of the nipple and areola has several features that suggest

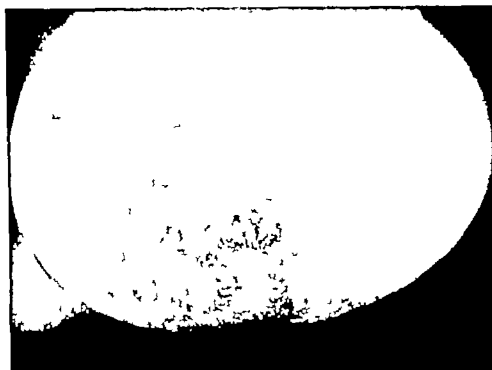


Fig 300 Dermatitis involving the areola only

its benign nature One of these is its rapid evolution Within a few weeks it extends to involve a large portion of the areola Figure 301 shows such a lesion

The patient, Mrs. I B a Santo Dominican woman aged 22, came to me with this crusted, moist, granular reddish lesion involving the nipple and almost the whole areola. She had had it for three months. The nipple was normal in shape. There was no tumor in the breast. A variety of ointments had not helped the lesion.

I biopsied it and proved that it was merely dermatitis Cultures of the lesion grew out a pure hemolytic staphylococcus coagulase positive The application of a mild anti septic ointment promptly cleared the lesion up

Paget s carcinoma evolves very slowly in comparison to benign dermatitis Many months would be required for Paget s erosion to extend over as wide an area as shown in Figure 301

A second feature of benign dermatitis is that it does not destroy the nipple

patients are often sent from one physician to another, frequently to dermatologists, and all sorts of misguided therapy—salves, cauterization, irradiation—are given without the true nature of the nipple erosion being discovered In our own department of dermatology the diagnosis has often been missed It is, of course, true that surgeons also sometimes fail to diagnose Paget's carcinoma, but in my experience dermatologists have been guilty more often than any other group of specialists

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			Number	Per cent	
Nipple erosion only	28	16 2	16	57 1	16 5
Nipple erosion and breast tumor	40	15 4	20	50 0	15 6
Breast tumor only	22	13 4	7	31 8	26 6
Total	90	15 2	43	47 8	17 9
Personal series of cases Breast carcinoma (all types) 1943–54	546	7 5	115	21 1	12 5

I saw her for the first time seven months after her initial symptom The surface of the nipple showed a moist, bright red, granular erosion, measuring 1 cm in diameter The breast was otherwise normal No tumor was palpable There were no enlarged axillary or supraclavicular lymph nodes

A 5 mm wedge of the erosion was excised under Novocain anesthesia It showed Paget's carcinoma in the epidermis There was some squamous metaplasia of the carcinoma cells which was interpreted as the result of the irradiation

Radical mastectomy was performed Intraductal carcinoma was found in 20 of 21 nipple ducts, but nowhere else in the breast There were no metastases in 31 axillary lymph nodes

Paget's carcinoma is most often mistaken for dermatitis of the nipple and areola It is true that dermatitis, sometimes of the contact type due to irritation from clothes or cosmetics, sometimes due to bacterial infection, sometimes of

the only form of breast carcinoma that may properly be biopsied in the physician s office. All other forms should be biopsied, as I have already emphasized in the hospital operating room with all preparations made for radical mastectomy

It is also essential to biopsy erosions of the nipple to protect the patient against the surgeon s error of mistaking dermatitis for carcinoma and performing unnecessary mastectomy Figure 302 shows an entirely benign dermatitis involving the nipple and the upper portion of the areola which had been present for one month. It was a crusted exudative lesion The attending surgeon mistakenly

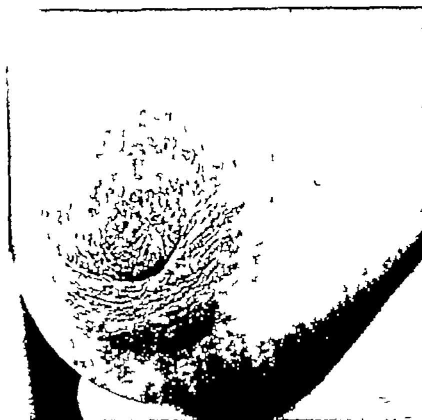


Fig 302. Dermatitis mistaken for Paget s carcinoma.

assumed that it was Paget s carcinoma and performed radical mastectomy without preliminary biopsy

Treatment

If the concept of the pathology of Paget s carcinoma which I have presented is accepted—namely that it is merely intraductal carcinoma involving the nipple ducts as well as the duct system of the breast itself—its treatment must be the same as that for other breast carcinomas There can be no logical defense for local excision or irradiation of the nipple lesion or for simple mastectomy These procedures have often been done for Paget s carcinoma, and even today continue to be advocated in some quarters. Local excision will fail to remove the carcinoma found so often in multiple foci in the breast. Simple mastectomy will fail to remove axillary metastases of the carcinoma Table 87 shows the fre

In cases of Paget's carcinoma that have extended out over the areola and to the skin of the breast the nipple is usually flattened and contracted by the fibrosis accompanying the carcinomatous infiltration

Another condition that must be distinguished from Paget's carcinoma is benign intraductal papilloma of the nipple This type of papilloma grows in the nipple ducts and sometimes projects out from them on the nipple surface as a reddish, granular, weeping lesion Like Paget's carcinoma the lesion appears on the nipple surface But unlike Paget's carcinoma, it forms a palpable mass that can be felt and often seen within the nipple Jones has recently written a good description of this form of papilloma

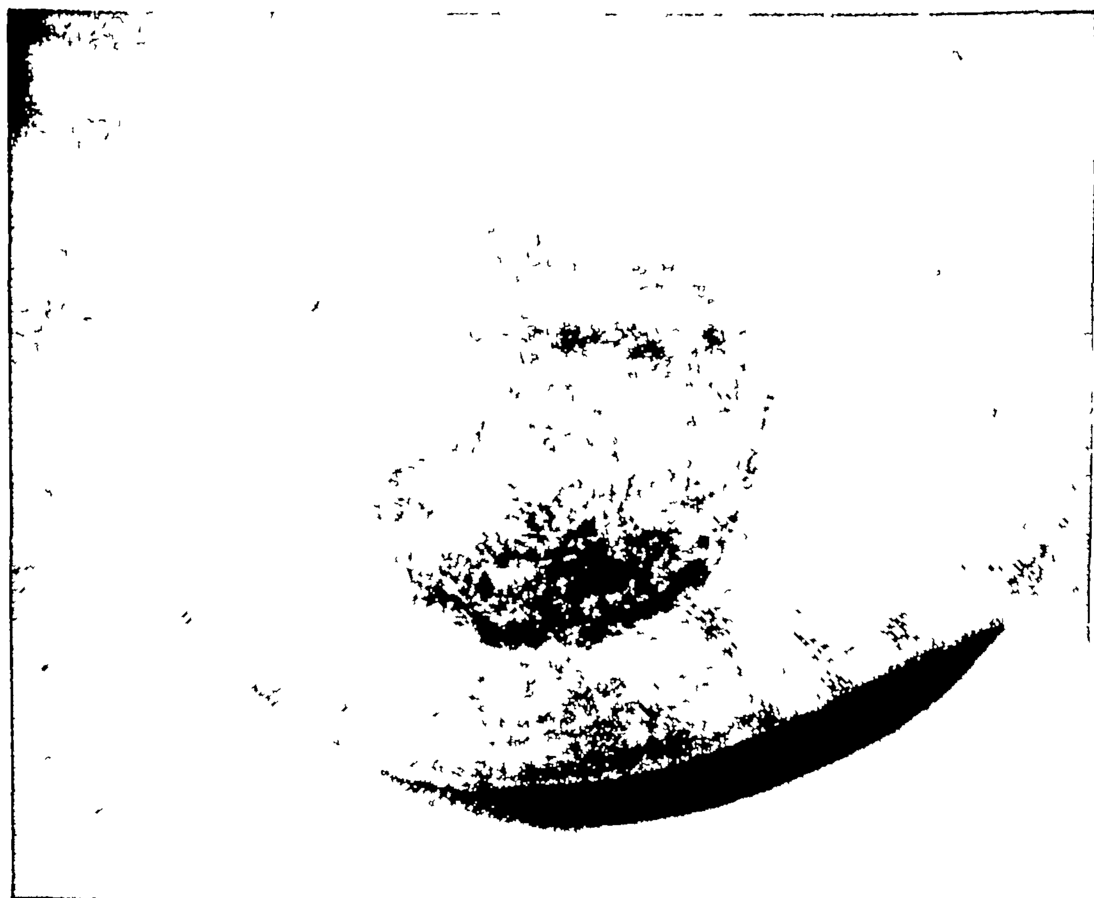


Fig 301 Dermatitis involving both nipple and areola

Infrequently, women whose nipples have been long inverted will develop maceration and irritation of the nipple epidermis, and a discharge This condition has no real similarity to Paget's carcinoma, and a routine of everting and cleaning the nipple will promptly correct it

The solution to the problem of prompt recognition of Paget's carcinoma is, of course, biopsy Every erosion of the nipple should be at once biopsied, no matter how minute and seemingly inconsequential it may be If this simple rule were followed, Paget's carcinoma would often be diagnosed in its early stage and it would become the most favorable form of breast carcinoma

The biopsy can properly be done in the office The base of the nipple is infiltrated with Novocain and a small wedge, about 5 mm in width, of the erosion is excised A single silk suture across the incision controls the bleeding This is

completely destroying it Meanwhile the carcinoma that is usually present in the depths of the breast continues to progress

The following case history illustrates the deceptive effect of irradiation on Paget s carcinoma

Mrs. B J a housewife aged 50 came to me in May 1954 for an erosion of the nipple Seven years previously in 1947 she had first developed a small erosion of the left nipple She had consulted a surgeon who assured her the lesion was benign and sent her to a radiotherapeutist colleague. He treated the nipple with an unknown amount of irradiation The lesion never entirely healed It broke open at intervals and itched occasionally Seven years later she finally came to me because her internist questioned the nature of the erosion

The epithelium of her left nipple was thin and atrophic and in its center there was a 3 mm. erosion. There was no palpable tumor in the breast and no enlarged axillary lymph nodes I biopsied the nipple erosion and found characteristic Paget s cells in the epidermis. A radical mastectomy was done which showed intraductal carcinoma both in the nipple and in the breast, and metastasis in one axillary lymph node

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quency of axillary metastases in the 70 patients in our Presbyterian Hospital series of cases of Paget's carcinoma treated by radical mastectomy

Even in the group of patients whose only clinical manifestation of Paget's carcinoma was a nipple erosion, the clinical group in which the disease is certainly *in its earliest stage, one patient among a total of seventeen had axillary metas-*

Table 87 Axillary Metastases According to Clinical Group in 70 Patients with Paget's Carcinoma Treated by Radical Mastectomy
(Presbyterian Hospital, 1915–1955)

Clinical group	Number of cases	Cases with axillary metastases	
		Number	Per cent
Nipple erosion only	17	1	5 9
Nipple erosion and breast tumor	33	20	60 6
Breast tumor only	20	12	60 0
All Paget's carcinoma	70	33	47 1
All breast carcinoma, Presbyterian Hospital, 1915–1942	1135		61 8

tases And in the group of patients with both nipple erosion and a palpable tumor, 60 6 per cent had axillary metastases These facts concerning the natural history of Paget's carcinoma do not justify treatment by any method other than radical mastectomy

Radical mastectomy is particularly successful in the cases of Paget's carcinoma in which there is no palpable tumor in the breast The results of the operation in 52 Presbyterian Hospital cases of Paget's carcinoma are shown in Table 88.

Table 88 Results of Radical Mastectomy in Paget's Carcinoma
(Presbyterian Hospital, 1915–1949)

Type	Number of cases	Cases with axillary involvement		Five year clinical cures	
		Number	Per cent	Number	Per cent
Nipple erosion only	9	1	11 1	6	66 7
Nipple erosion and breast tumor	31	19	61 3	14	45 2
Breast tumor only	12	8	66 7	5	41 7
Total	52	28	53 8	25	48 1

The 66 7 per cent five year cure rate for the patients with only a nipple erosion can be contrasted with the relative clinical cure rate of 49 7 per cent for ordinary breast carcinoma in our Presbyterian Hospital 1935–1942 series of cases

Radiotherapy to the nipple lesion is a dangerous method of treating Paget's carcinoma because it often holds the superficial nipple lesion in check without

As Table 89 indicates, the disease developed during pregnancy in 4 of our patients Summaries of these cases follow

Table 89 Inflammatory Carcinoma During Pregnancy or Lactation

Author	Year	Number of cases	Number developing during pregnancy or lactation
Lee and Tannenbaum	1924	28	0
Taylor and Meltzer	1938	38	1
Meyer Dockerty and Harrington	1948	74	1
Chris	1950	20	0
Presbyterian Hospital	1955	58	4

Mrs K. M aged 25 noted a small tumor of her left breast during the sixth month of her first pregnancy When examined six weeks after delivery the breast was four or five times its normal size, generally indurated, and the skin over two-thirds of its surface was red and edematous There were large nodes in both axillæ After biopsy to prove the carcinomatous nature of the lesion it was irradiated but she died after five months

Mrs. M O M aged 40 discovered a tumor of her right breast three weeks after she began to nurse her third baby When she came for treatment fourteen months later the tumor had grown to 11 cm. in diameter the skin over the lower half of the breast was edematous and red, and there were large axillary and supraclavicular nodes One of these was removed and showed carcinoma. Despite irradiation she died six months later

Mrs. K. H. aged 33 found a tumor in her left breast during the second month of her fifth pregnancy When she was admitted to the hospital two months later the tumor measured 9 cm. in diameter and there was extensive edema and redness of the skin over the breast and moderate enlargement of axillary nodes. Radical mastectomy was done but she died seven months later

Mrs. A. R. aged 31 developed a tumor of her left breast during the first month of her sixth pregnancy After delivery she attempted to nurse but the tumor enlarged and redness and edema of the skin developed over it It was diagnosed as an abscess and incised. Its carcinomatous nature was discovered only after the incision failed to heal. Radical mastectomy was then done. She developed local recurrence and died with pulmonary metastases forty months after operation, and fifty two months after her tumor had been discovered.

Symptoms

The inflammatory type of breast carcinoma, like other breast carcinomas usually makes itself manifest by a tumor Table 90 which lists the presenting symptoms, as well as the earliest symptoms, in our 58 Presbyterian Hospital cases of inflammatory breast carcinoma, shows that in 36 or two-thirds of our patients a tumor was one of the earliest symptoms

The further course of these patients with inflammatory carcinoma whose disease begins with a tumor is very different, however from that of patients with the usual breast carcinoma After a short time often not more than a few weeks symptoms suggesting inflammation develop The entire breast becomes enlarged and indurated The skin over it becomes red and edematous and abnormally warm. The diseased breast *is often painful*—an uncommon symptom in ordinary breast carcinoma.

CHAPTER 24

INFLAMMATORY CARCINOMA

Our systematized knowledge of this, the most terrible form of breast carcinoma, is relatively recent Toward the end of the last century several surgeons of great experience, including Billroth and von Volkman, had noted the exceptional malignancy of breast carcinomas evolving during pregnancy and had coined for them the term "mastitis carcinomatosa " Schumann, in 1911, described in detail a case of acute carcinoma mistaken for an abscess in a lactating breast, and collected the earlier case reports Most of these cases were not examples of the disease that we today call inflammatory carcinoma, but the name "mastitis carcinomatosa," and the implied association with pregnancy and lactation, persisted and confused students of breast carcinoma until recently

The clinical picture of inflammatory carcinoma as we know it today was defined in two excellent papers, the first by Lee and Tannenbaum in 1924, and the second by Taylor and Meltzer in 1938 Their papers so well established the disease as a special form of breast carcinoma that it is today known in all surgical clinics If anything, the diagnostic criteria are interpreted too liberally and the diagnosis is made too frequently

Incidence

Between the years 1915 and 1949, 58 patients with breast carcinoma which I have classified as the inflammatory type were seen in the Presbyterian Hospital They constituted about 3 per cent of all patients with primary breast carcinoma coming to the hospital Inflammatory carcinoma, as we classify it, is therefore a comparatively rare disease It constituted 1 3 per cent of Lee and Tannenbaum's series of breast carcinomas, and 4 per cent of Taylor and Meltzer's series

Predisposing Factors

There was no predilection of the disease in our series of cases for patients of a special race or age The average age of our patients with inflammatory carcinoma was 47, or about three years less than the average age for all our Presbyterian Hospital patients with breast carcinoma Similarly, in Taylor and Meltzer's series of cases of inflammatory carcinoma the age distribution of the patients was the same as for breast carcinoma in general

Pregnancy and lactation do not predispose to the inflammatory type of carcinoma, as early writers thought Table 89 summarizes the association of pregnancy and lactation in the larger modern case series

the entire breast In the axilla there was a chain of large firm nodes extending high up and fixed to the underlying chest wall

The surgeon in charge of the patient although realizing that her carcinoma was advanced performed a so-called "palliative radical mastectomy He did not achieve palliation, however for local recurrence developed within five months and two months later a similar inflammatory carcinoma developed in the left breast Left simple mastectomy was done but it did not check the progress of her disease. She died seven months after onset of her symptoms.

In the 37 patients in our case series in whom the examiner described a dominant tumor of the breast the tumor was often very large Its average diameter was 83 mm as compared with an average diameter of 48 mm. for 668 primary breast carcinomas measured clinically in our 1935–1942 Presbyterian Hospital series



Fig 303 The inflammatory type of carcinoma of the breast.

The redness of the skin which is the most distinctive feature of inflammatory carcinoma, is not always a bright red It is sometimes merely a flush of pink. The discoloration is not uniform over the breast. It tends to be more prominent over the most dependent part of the breast and it is often mottled in its distribution We have not counted small zones of redness as constituting part of the syndrome of inflammatory carcinoma For example, the skin over a limited area immediately over a rather superficial carcinoma is not infrequently red and should not be regarded as a sign of inflammatory carcinoma It is merely a local reaction to the underlying invasive or necrotic carcinoma In a general way we have regarded as significant in terms of inflammatory carcinoma only *redness that* involves more than one third of the skin over the breast The redness is very extensive in some cases, involving the skin of the opposite breast as well as the lateral and posterior chest

In about one-fourth of our patients with inflammatory carcinoma the disease began, not with a localized tumor but with symptoms suggesting inflammation—pain and tenderness, generalized enlargement or induration of the breast, and redness and increased warmth of the skin In this group of patients the first diagnosis made has usually been infection

Table 90 Presenting Symptoms in 58 Cases of Inflammatory Carcinoma
(Presbyterian Hospital 1915–1949)

		Symptoms recorded	Recorded as an early symptom
1	Localized tumor	37	36
2	Pain in breast or nipple	22	12
3	Enlargement of breast	19	14
4	Redness	22	8
5	Tenderness on pressure	7	5
6	Generalized hardness	6	4
7	Increased warmth of skin	5	2
8	Edema of skin	5	1
9	Nipple discharge	6	1
10	Nipple retraction	7	1
11	Itching of nipple	3	1
12	Axillary tumor	8	3
13	Pain in axilla	4	1
14	Swelling of arm	1	1
15	Bone pain	1	—

Our patients with inflammatory carcinoma came for treatment earlier than patients with other forms of breast carcinoma The average duration of symptoms on admission in our 58 patients with inflammatory carcinoma was only five months, as compared with an average duration of 10 7 months for our 1,544 patients with primary breast carcinoma seen at the Presbyterian Hospital between 1915 and 1942

Physical Features of Inflammatory Carcinoma

The essential clinical characteristics of the inflammatory type of carcinoma in its fully evolved state are enlargement and generalized induration of the breast, and redness and edema of the skin over it All these features were eventually evident in all the cases that we have classified as inflammatory carcinoma In 37 of the patients a single dominant tumor rather than generalized induration of the breast was present on admission

Figure 303 shows the characteristic appearance of inflammatory carcinoma

The patient, Mrs N C, aged 46, noticed that her right breast was enlarging three months before she came to the Presbyterian Hospital On admission the right breast was elevated in position on the chest wall, and formed a bulky, solid, firm mass fixed to the deeper structures The skin over the lower portion of the breast was bright red, and there was reddish mottling of the skin over the remainder of the breast The outline of the lower portion of the areola was lost in the red discoloration

The nipple was flattened and broadened There was edema of the skin over almost

Differential Diagnosis

Abscess. The resemblance of inflammatory carcinoma to true inflammation is so close that it is often mistaken for, and treated as, an abscess. The chief distinguishing features of an abscess are that the signs of inflammation in the breast that accompany it are apt to be more localized than in inflammatory carcinoma, and that abscess is usually accompanied by leucocytosis and fever, which are infrequent in inflammatory carcinoma. It should be remembered also that true abscess ordinarily occurs only in lactating breasts or shortly after cessation of lactation. I have already indicated the rarity of inflammatory carcinoma in association with lactation.

Duct Ectasia. In the advanced stage of the evolution of duct ectasia in which the irritative material has penetrated the duct walls and set up inflammation and even abscess in the breast, the process may suggest inflammatory carcinoma. These patients with duct ectasia are, like those with inflammatory carcinoma, older women, and their disease is not associated with lactation. The most important difference between the two diseases is that the signs of inflammation produced by duct ectasia are apt to be more localized and more chronic than those accompanying inflammatory carcinoma.

Redness and Edema of the Skin due to Necrosis of Carcinoma. In occasional patients with large carcinomas of the breast, redness and edema of the skin may develop merely as a result of spontaneous necrosis in the tumor, and without being indicative of the inflammatory type of carcinoma. In such patients the redness and edema are usually comparatively limited in extent and are localized over the tumor. The phenomenon of redness due to necrosis is more apt to occur in the circumscribed type of carcinoma than in other types. The poor blood supply of the broad masses and strands of carcinoma cells in these tumors may be a factor. The following case is an example.

Mrs. L. M., a 54 year old woman, was admitted to the Delafield Hospital for a tumor of the right breast that she had first noted only five weeks previously. It had grown more rapidly and had become painful during the last three weeks.

Examination showed the right breast to be half again as large as the left, due to the presence of a 10 cm. hard tumor filling its center. The tumor was somewhat fixed to the underlying chest wall. The skin over the tumor was reddened, and over the lower half of the breast it was edematous. There were two 1 cm. enlarged, firm axillary nodes.

The lesion was classified as inflammatory carcinoma. Irradiation was decided upon, and to facilitate delivering the desired tumor dose the radiotherapeutists requested simple mastectomy. This was performed, the lower axillary lymph nodes being included in the dissection. Pathological study of the specimen showed that the tumor occupied the center of the breast, was well delimited from the surrounding breast tissue, and was made up of soft, lobulated, yellowish-pink tissue. At its center there was a large cavity lined by necrotic tissue and filled with cloudy amber fluid. The tumor proved to be the circumscribed type of carcinoma, with extensive necrosis. It showed some squamous metaplasia. There were no metastases in 13 lymph nodes.

Irradiation treatment was completed without incident. The patient had no further evidence of breast carcinoma. She died two years later from carcinoma of the uterus.

This case, then, is one in which the large breast tumor and the redness and the edema of the overlying skin were not due to inflammatory carcinoma but to necrosis in a bulky circumscribed type of carcinoma.

The reddened skin in these patients often feels abnormally warm to the touch This evidence in our series of cases cannot be evaluated very well since there were many different examiners Unfortunately, no accurate skin temperature measurements were made in our cases

The edema of the skin that accompanies the redness of course indicates blockage of the subdermal lymphatics by carcinoma Edema, also, has been of considerable extent in the cases that we have classified as inflammatory carcinoma, usually involving more than one-third of the skin over the breast

Retraction of the nipple is often evident in these patients with inflammatory carcinoma, the retracted nipple being surrounded by edematous and reddened skin Nipple retraction was noted in 57 per cent of our patients

Physiological signs of inflammation—elevated body temperature and leucocytosis—occur in very few of these patients with inflammatory carcinoma In Taylor and Meltzer's series of 38 cases there were only 5 patients who had leucocytosis, and 6 who had a febrile course The latter, however, all had some complication that might have been responsible Similarly, in our series of patients there were only a few whose blood count or temperature was abnormal Only one of 39 patients in whom a blood count was done had leucocytosis Two of the patients had elevation of body temperature

Axillary metastases are a regular feature of inflammatory carcinoma Fifty-six of our 58 patients had clinical involvement of axillary nodes on admission, and in half of them the involvement was massive By this we mean that the involved nodes measured more than 2 5 cm in their greatest transverse diameter In the 29 patients who were treated by radical mastectomy, making microscopical study of the nodes possible, all were found to have axillary metastases

More distant metastases were found in 18 of our 58 patients on admission Eleven had palpable subclavicular nodes, three pulmonary metastases, and four bone metastases The opposite breast was involved in one of our patients on admission, and became involved during the course of the disease in at least 11 other patients In Taylor and Meltzer's series of 38 cases, 21 ultimately developed involvement of the opposite breast

In 56 of our 58 patients with inflammatory carcinoma, the end results are known All succumbed to their disease Most of them died with uncontrolled local disease and widespread regional lymph node, visceral, and bone metastases The course of their disease was abnormally rapid, as compared with other forms of carcinoma of the breast The average duration of the disease in our patients with inflammatory carcinoma, from the first symptoms until death, was 20 months The shortest duration in any patient was one month, and the longest duration 68 months In Taylor and Meltzer's series of cases the average duration of disease was 12 3 months Our average duration of approximately 20 months is considerably shorter than the average duration of untreated carcinoma of the breast in general which, in Wade's collected series of 777 cases, was 38 55 months

Treves has described three examples of the inflammatory type of carcinoma in males The course of the disease in these male patients was no different from the course of the disease as I have described it in females

Fig 304 Large cell type of carcinoma of the breast filling up dilated lymphatics in the breast in a case of inflammatory carcinoma.



Fig 305 Carcinoma in a skin lymphatic in inflammatory carcinoma

Carcinoma En Cuirasse. Although carcinoma *en cuirasse* produces reddish discoloration of the skin, its resemblance to inflammatory carcinoma goes no further. *En cuirasse* is a very slow process in which the skin is thickened and fibrosed as the carcinoma advances in its deeper portion. There is no edema of the skin, and no acute signs suggesting inflammation.

Lymphoblastoma. Leukemic or lymphosarcomatous involvement of the breast can resemble inflammatory carcinoma very closely. The differentiation can be made only by biopsy.

Pathology

Because most of the patients with inflammatory carcinoma are not operated upon, information concerning the pathological characteristics of the lesion has been slow to accumulate. The studies of Hartmann and his associates, of Taylor and Meltzer, of Meyer, Dockerty and Harrington, and of Chris are in agreement, however, that inflammatory carcinoma is not a special microscopic type. All the usual microscopic forms of carcinoma are found.

Our Presbyterian Hospital series of cases of inflammatory carcinoma, like these others, was made up of a wide variety of microscopic types. There were partly intraductal carcinomas, circumscribed carcinomas, scirrhous carcinomas, small cell carcinomas, and large cell carcinomas. A few formed mucin. Of the 33 tumors which we were able to study adequately microscopically, 1 was well differentiated, 10 were moderately differentiated, and 22 were classified as undifferentiated. If it were possible to say that any single type of carcinoma predominated it would be the large cell type. The cells in this type have large pale cytoplasms, and prominent nuclei showing bizarre variation in size and shape. They form loosely arranged masses, without any intercellular fibrous stroma. There were 9 such carcinomas among the 30 in our series. Figure 304 shows the cells of 1 of these large cell carcinomas growing in dilated lymphatics in the breast.

One of the questions that arises concerning the histology of inflammatory carcinoma is how often these tumors show any microscopical evidence of the "inflammation" that characterizes them clinically. In our series of thirty there were only three in which there was an unusual degree of lymphocytic infiltration in and about the carcinoma.

The redness of the skin over the breast that characterizes this disease, like the edema that accompanies the redness, finds its explanation microscopically in the involvement of the subdermal lymphatics by the carcinoma. When the skin and subcutaneous tissue are adequately studied microscopically, emboli of carcinoma cells will almost always be found in the superficial lymphatics. Figure 305 shows this phenomenon in one of our inflammatory carcinomas. Presumably, the redness of the skin is due to hyperemia in response to the presence of the carcinoma close beneath it. It may be asked why, then, is redness of the skin not always present when edema of the skin develops, as it does in a good many locally advanced carcinomas. I cannot answer this question except to suggest that the peculiarly malignant nature of these inflammatory carcinomas in some manner induces hyperemia of the skin.

The subdermal lymphatics are not the only ones involved in inflammatory

carcinoma were treated by radical mastectomy Local recurrence is known to have developed in 68.3 per cent There were no five year cures and only one patient survived longer than five years She was a woman aged 49 who developed local recurrence and distant metastases following radical mastectomy but irradiation held her disease in check for a considerable time. She died 78 months after the onset of her disease and 68 months after her operation The course of the disease in this patient was certainly not typical of that of inflammatory carcinoma The typical story of our patients treated by radical mastectomy is exemplified by the following case history

Mrs. L. W was a housewife aged 56 Three weeks before her admission to the Presbyterian Hospital she had developed throbbing and shooting pain in her right breast. It radiated to the axilla. With the onset of the pain she noted that her right nipple was retracted and that the skin around it was reddened, and the breast was enlarged

Examination showed that the right breast was larger than the left and diffusely indurated. No definite localized tumor could be felt. The nipple was inverted and there was extensive redness and edema centered around the areola and involving at least one-half of the skin over the breast. A 1 5 cm. hard right axillary lymph node suggested metastasis The disease was classified as inflammatory carcinoma.

Radical mastectomy was nevertheless done. Pathological study showed the lesion to be a highly anaplastic carcinoma that had metastasized to 8 of 21 lymph nodes She was given postoperative irradiation but nevertheless local recurrence in the lateral skin flap was noted thirteen months after operation Pulmonary metastasis became apparent two months later She died sixteen months after operation

Although operation failed to cure any of our patients with inflammatory carcinoma we may ask whether it prolonged or shortened life We find it impossible to answer this question from our data shown in Table 91 Study of the

Table 91 Inflammatory Carcinoma Length of Survival in 56 Patients Followed Until Death (Presbyterian Hospital 1915–1949)

Treatment	Number of patients	Months of survival following treatment			Average survival from earliest symptom noted
		Shortest survival	Longest survival	Average survival	
Radical mastectomy	29	3 0	68 0	19 5	25 9
Other	27	1 0	27 0	10 1	13 6
Total	56	1 0	68 0	15 2	20

case histories reveals beyond question that the patients with less advanced disease were operated upon This probably accounts for the fact that the average total duration of the disease in the patients treated by operation was 25.9 months as compared with 13 6 months for patients not operated upon

When no cures can be expected, and no definite evidence of prolongation of life can be shown it seems to me entirely unreasonable to treat these patients by radical mastectomy Meyer Dockerty and Harrington continue to advise

carcinoma Emboli are often seen in the lymphatics of the breast itself (Fig 306) We found them in two-thirds of our cases of inflammatory carcinoma, which is a good deal more frequent than in ordinary breast carcinoma We also noted several examples of emboli in blood vessels These are further indications of the extraordinary malignancy of the inflammatory type of carcinoma

Treatment

The papers by Lee and Tannenbaum, and Taylor and Meltzer, not only defined inflammatory carcinoma as a clinical entity, but they established the fact that the disease cannot be cured by surgery Previously the surgical tradition of operating on all breast carcinoma had been applied with disastrous results to inflammatory carcinoma

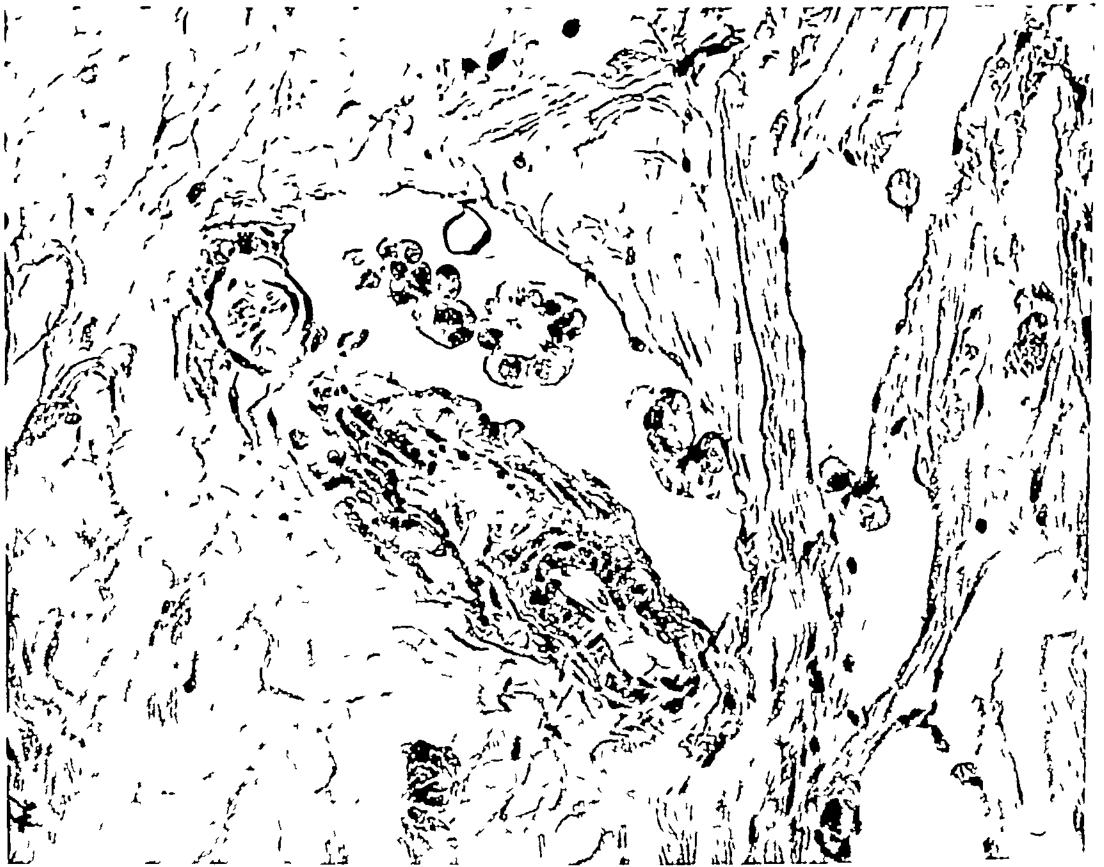


Fig 306 Emboli of carcinoma cells in breast lymphatics in inflammatory carcinoma

Lee and Tannenbaum reported that radical mastectomy in their four patients with inflammatory carcinoma was followed by prompt local recurrence and early death The fate of Taylor and Meltzer's six patients treated by radical mastectomy was the same

Our Presbyterian Hospital experience has provided good data regarding the futility of surgical attack upon inflammatory carcinoma Because some of our attending surgeons have remained unconvinced of the incurability of the disease by operation, radical mastectomy has continued to be done for some of these patients in our hospital, thus providing a good test of surgical therapy

Between 1915 and 1949 a total of 29 patients with the inflammatory type of

carcinoma were treated by radical mastectomy Local recurrence is known to have developed in 68 3 per cent There were no five year cures, and only one patient survived longer than five years She was a woman aged 49 who developed local recurrence and distant metastases following radical mastectomy but irradiation held her disease in check for a considerable time She died 78 months after the onset of her disease, and 68 months after her operation The course of the disease in this patient was certainly not typical of that of inflammatory carcinoma The typical story of our patients treated by radical mastectomy is exemplified by the following case history

Mrs. L. W was a housewife aged 56 Three weeks before her admission to the Presbyterian Hospital she had developed throbbing and shooting pain in her right breast. It radiated to the axilla With the onset of the pain she noted that her right nipple was retracted and that the skin around it was reddened, and the breast was enlarged.

Examination showed that the right breast was larger than the left and diffusely indurated No definite localized tumor could be felt. The nipple was inverted and there was extensive redness and edema centered around the areola and involving at least one-half of the skin over the breast A 1.5 cm. hard right axillary lymph node suggested metastasis The disease was classified as inflammatory carcinoma.

Radical mastectomy was nevertheless done. Pathological study showed the lesion to be a highly anaplastic carcinoma that had metastasized to 8 of 21 lymph nodes. She was given postoperative irradiation but nevertheless local recurrence in the lateral skin flap was noted thirteen months after operation Pulmonary metastasis became apparent two months later She died sixteen months after operation.

Although operation failed to cure any of our patients with inflammatory carcinoma we may ask whether it prolonged or shortened life We find it impossible to answer this question from our data, shown in Table 91 Study of the

Table 91 Inflammatory Carcinoma Length of Survival in 56 Patients Followed Until Death (Presbyterian Hospital 1915-1949)

Treatment	Number of patients	Months of survival following treatment			Average survival from earliest symptom noted
		Shortest survival	Longest survival	Average survival	
Radical mastectomy	29	3 0	68 0	19 5	25 9
Other	27	1 0	27 0	10 1	13 6
Total	56	1 0	68 0	15 2	20

case histories reveals beyond question that the patients with less advanced disease were operated upon This probably accounts for the fact that the average total duration of the disease in the patients treated by operation was 25 9 months as compared with 13 6 months for patients not operated upon

When no cures can be expected and no definite evidence of prolongation of life can be shown it seems to me entirely unreasonable to treat these patients by radical mastectomy Meyer Dockerty and Harrington continue to advise

operation, basing their recommendation upon the fact that 3 of their 63 patients operated upon survived five years Studying their data, however, leaves me in some doubt that all of their patients actually had the inflammatory type of carcinoma They stated that the skin over the breast was described as being red in only 73 per cent of their cases, and edematous in only 78 per cent of their cases In our case material I have classified as inflammatory carcinoma only the cases in which both of these features were present

The results of irradiation have been disappointing in our patients with the inflammatory type of carcinoma Carcinoma in large breasts has always been a difficult problem for the radiotherapeutists, and these patients with inflammatory carcinoma have done particularly badly The primary lesion in the breast, and the axillary nodes, have diminished somewhat in size in a few of the patients, but the disease has progressed so rapidly in most of them that it has always been beyond the control of the radiotherapeutist We have come to the pessimistic point of view of not attempting to give these patients intensive irradiation because it has regularly proved futile

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CHAPTER 25

SPECIAL PATHOLOGICAL FORMS OF BREAST CARCINOMA

The special clinical features of papillary carcinoma, Paget s carcinoma, and inflammatory carcinoma set them apart from other breast carcinomas The great majority of breast carcinomas possess no such characteristic clinical features They do indeed, show a great range in growth vigor but we cannot classify them in this regard according to any generally accepted standards

From the clinical point of view we can only group all other breast carcinomas together and hope to sort out from among them, as our correlation of clinical characteristics with pathological features improves, additional characteristic types of breast carcinoma.

This paucity of clinical types of breast carcinoma should not deter us from attempting to classify breast carcinomas as to their gross pathological and histological forms. In the present chapter I shall attempt this

Classification According to Site of Origin

At first thought we might assume that if we could accurately classify carcinomas of the breast as to their site of origin in the breast epithelium we might hope to single out characteristic clinical types Unfortunately attempts at this kind of classification have not proved very helpful One of the greatest students of breast carcinoma, E. K Dawson has concluded that malignant epitheliosis (carcinoma) has its primary site always in the ducts, and, in the majority of cases in the terminal intralobular ducts Involvement of the ductules (acini) is not primary but secondary and is evidence of extension of the cancerous process

Another distinguished Scottish pathologist, Robert Muir has traced the origin of breast carcinoma to the acinar epithelium as well as the duct epithelium. He has named the former type intra acinous carcinoma, but has not ascribed to it any special clinical characteristics

Stewart, whose Fascicle 34 in the Atlas of Tumor Pathology of the Armed Forces Institute of Pathology is one of the best recent attempts at classification of breast carcinoma, regards the duct epithelium as the site of origin for the great majority of carcinomas He does however trace the origin of a small percentage of breast carcinomas, to which he gives the name of *lobular carcinoma* to the epithelium of the acini in the mammary lobules. In Stewart s lobular mammary carcinoma in situ the lobules in which the process evolves are enlarged but retain in general, a configuration like the mammary lobule The

acinar lumens are usually obliterated The proliferating cells that fill them, although of the approximate size of normal acinar epithelial cells, vary more in size and shape and are more hyperchromatic than normal cells Mitoses are not significantly increased in number These cells suggest a malignant character, but it is rather the architecture of the lesion as a whole than the cytology that makes the diagnosis In a more fully evolved stage of the lesion, which Stewart calls "infiltrating lobular carcinoma," the lobular configuration is lost and the small cells string out in a fibrous matrix Stewart does not ascribe any special clinical character to lobular carcinoma, except that in advising only simple mastectomy for his non-infiltrating in situ type he of course suggests that it has less tendency to metastasize than ordinary infiltrating carcinoma I shall refer to this question again

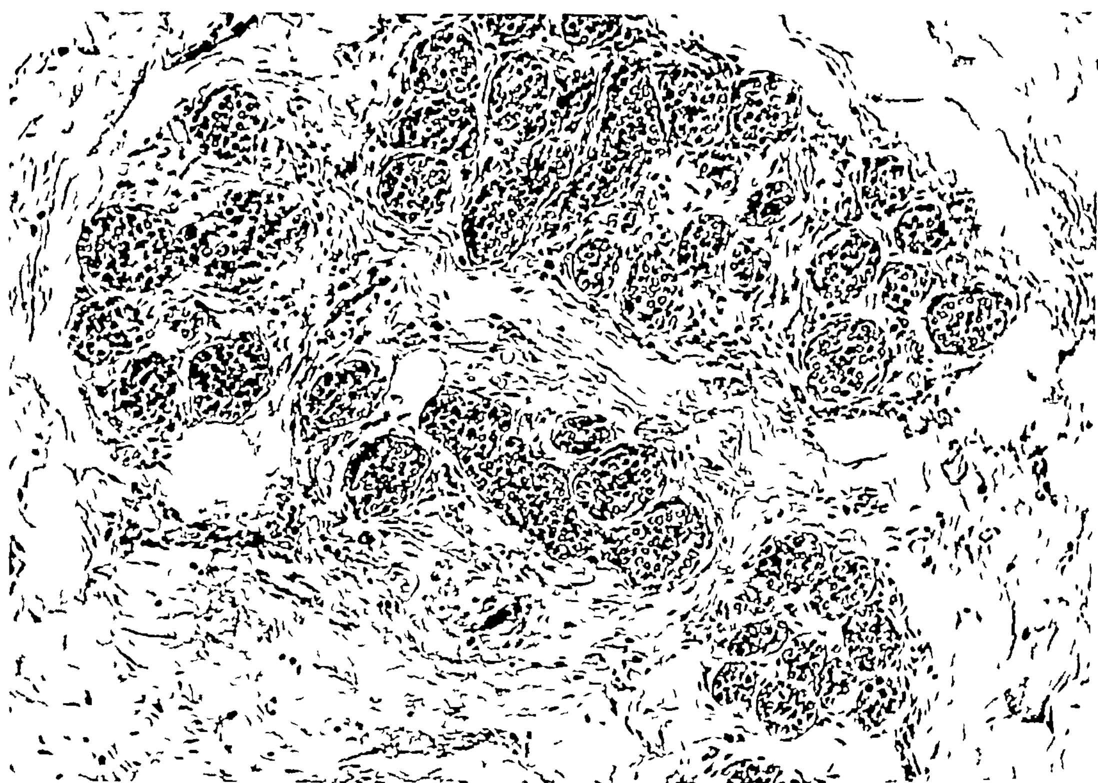


Fig 307 "Lobular" carcinoma, showing a configuration suggesting the mammary lobule

We have occasionally seen, in our laboratory, breast carcinomas that fit Stewart's description of "lobular carcinoma in situ," but we have not felt certain that they originated from the acinar epithelium and, what is more important, that they were non-infiltrating The lesion that Stewart classifies as "infiltrating lobular carcinoma" is well known to us, and we have usually called it small cell carcinoma The histogenic classification of this group of infrequent carcinomas of the breast is most difficult, but we cannot deny that their architecture sometimes suggests an origin from the lobule Figures 307 and 308 show such a carcinoma from our collection Its lobular architecture is shown in low power in Figure 307, and its cytology in higher power in Figure 308 We have not been able to define any special clinical characteristics for this infrequent type of carcinoma

Histological Classification

All other breast carcinomas in our opinion originate from duct epithelium They can be classified only in terms of their histological character Our classification which follows, has been kept as simple as possible

1 Intraductal carcinoma
2 Circumscribed carcinoma
3 Mucoid carcinoma
4 Apocrine carcinoma
5 Carcinoma with squamous metaplasia
6 Carcinoma with osseous and cartilaginous metaplasia
7 Carcinoma (no special type)



Fig 308 Higher power view of "lobular" carcinoma.

It will be noted that in our classification we do not include a division into non-infiltrating and infiltrating types of carcinoma, as Stewart has done for papillary comedo and lobular carcinoma. We believe that all these lesions are fully malignant carcinomas, capable of metastasizing and killing. The fact that we do not see, in the study of an individual tumor any point at which the cells penetrate the duct wall, or invade the breast stroma, does not in our opinion justify the conclusion that infiltration has not taken place The exceedingly small portion of the total extent of the carcinomatous epithelium that we see in any individual carcinoma, even when many microscopical sections are studied can only suggest in a general way whether or not infiltration has actually occurred. It cannot be regarded as decisive evidence The statement by the pathologist that a carcinoma is "non infiltrating" is apt to be taken literally by the surgeon as an

acinar lumens are usually obliterated The proliferating cells that fill them, although of the approximate size of normal acinar epithelial cells, vary more in size and shape and are more hyperchromatic than normal cells Mitoses are not significantly increased in number These cells suggest a malignant character, but it is rather the architecture of the lesion as a whole than the cytology that makes the diagnosis In a more fully evolved stage of the lesion, which Stewart calls "infiltrating lobular carcinoma," the lobular configuration is lost and the small cells string out in a fibrous matrix Stewart does not ascribe any special clinical character to lobular carcinoma, except that in advising only simple mastectomy for his non-infiltrating in situ type he of course suggests that it has less tendency to metastasize than ordinary infiltrating carcinoma I shall refer to this question again

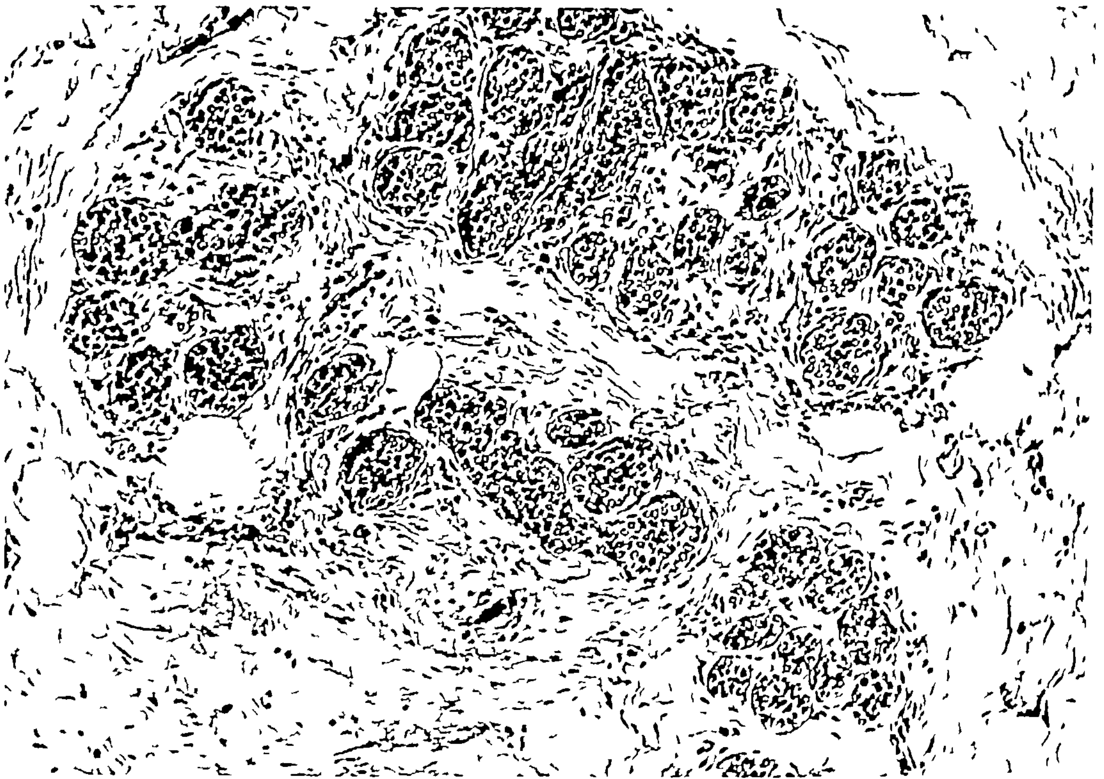


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2. *Solid intraductal carcinoma* In this form the ducts are solidly filled with lly viable carcinoma cells, as shown in Figure 311 The individual cells in this pe are apt to be smaller and more uniform in size and shape

3 *Cribriform intraductal carcinoma* In this form also the ducts are ompletely filled with carcinoma, but the cell masses have a cribriform pattern his kind of pattern may be found in occasional small isolated ducts in benign traductal epithelial proliferation But when it is seen in groups of considerably ilated ducts filled with proliferating cells as in Figure 312, it means carcinoma

The so-called adenoid cystic type of carcinoma which so closely resembles the ylindroma of salivary gland origin may be related to this form of intraductal arcinoma.



Fig 310 Comedo intraductal carcinoma.

4 *Low Papillary Intraductal Carcinoma* In this type the greatly dilated ducts are lined by carcinoma cells thrown up in very low papillary folds (Fig. 313) These projections into the duct lumens usually have no connective tissue cores The individual proliferating cells tend to be small and comparatively regular In some lesions they have acidophilic cytoplasms that suggest the pale epithelium of the mammary gland such lesions have sometimes been called sweat gland carcinoma.

These intraductal carcinomas with a low papillary pattern are not to be confused with the papillary carcinomas that I have described in Chapter 22. In the latter the papillary pattern is much more pronounced

The intraductal carcinomas that we have included in the present series were classified as such by Dr Stout himself in a special study that he made of the morphology of the breast carcinomas recorded in his laboratory between 1930

indication that he may perform something less drastic than a radical mastectomy In this way the patient's chance of cure may be lost

Intraductal Carcinoma

By intraductal carcinoma we mean the carcinomas that appear to grow predominantly within the mammary ducts The so-called comedo carcinoma is a prototype of intraductal carcinoma But there are a number of other cell patterns of intraductal growth We know that all are infiltrating and fully malignant even though we do not happen to see actual infiltration



Fig 309 The gross appearance of comedo intraductal carcinoma

Papillary carcinoma and Paget's carcinoma are also types of intraductal carcinoma, but they have clinical features that characterize them and justify considering them separately, as I have done in Chapters 22 and 23

Intraductal carcinoma, in the sense that I here consider it, includes several forms of intraductal growth grouped together, as follows

1. *Comedo intraductal carcinoma.* The ducts are dilated and filled with carcinoma cells The centers of these cell masses have become necrotic Grossly, the dilated ducts appear as small, yellowish-gray tubes from which the semi-solid necrotic plugs can be expressed as from a comedone of the skin (Fig 309) Microscopically, the viable cells that rim the ducts in this form of carcinoma are so large, and show such a high degree of variation in size and shape and such hyperchromatism, that their malignant nature is obvious (Fig 310)

and 1942 He classified tumors as intraductal only when at least 50 per cent of the carcinoma grew within ducts

Incidence Intraductal carcinoma is the most frequent of the several special forms of carcinoma that have no special distinguishing clinical features In his microscopical review Dr Stout classified 102 of a total of 668 carcinomas or about 15 per cent, as intraductal

The average age of our patients with the intraductal type of carcinoma was 46 years This is four years younger than the average age of patients with carcinoma of no special type in our hospital

Clinical Features The average duration of symptoms in our 102 patients with intraductal carcinoma was 7 5 months, which is not much different from

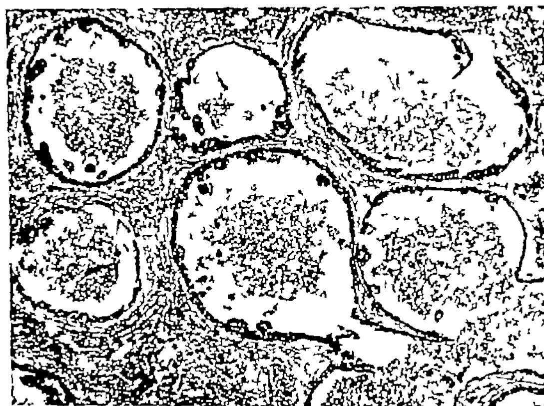


Fig 313 Low papillary intraductal carcinoma

the duration for ordinary carcinoma in our hospital during the same period of time

The average size of the intraductal carcinomas, measured clinically was 4 7 cm., which is almost the same as the size of ordinary breast carcinoma in our data

Axillary metastases were found in 62 per cent of our patients with intraductal carcinoma who had radical mastectomy This is almost the same frequency of axillary metastases as in carcinoma of no special type in our hospital

From these data it is evident that the intraductal carcinomas have no special distinguishing clinical features. I have had the impression that these carcinomas are somewhat less apt to produce a marked degree of retraction but I cannot document it

Fig 311. S[illegible] carcinoma



Fig 312. Cribriform intraductal carcinoma.

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Treatment. Radical mastectomy was more successful in our patients with intraductal carcinoma than in our patients with carcinoma of no special type The 5 year clinical cure rate was 57 8 per cent (Table 92) for the former, and 40 1

Table 92 102 Cases of Intraductal Carcinoma* Treated by Radical Mastectomy (Presbyterian Hospital, 1930 1942)

Average age at admission	46 years
Average duration of symptoms	7 5 months
Average clinical size of tumor	4 7 cm
Per cent with axillary metastases	62 1
Number of 5 year clinical cures	59
Per cent of 5 year clinical cures	57 8

* Cases with Paget's disease and papillary carcinoma not included

per cent for the latter These results confirm the generally held opinion that intraductal carcinoma is a less malignant type

The knowledge that the carcinoma which I have to deal with is an intraductal type and likely, therefore, to have a better prognosis, has sometimes influenced my decision as to treatment, as in the following case

Mrs N O, aged 41, had first discovered a small tumor in her right breast four months previously The tumor was situated just below and lateral to the nipple Her family physician diagnosed it "mastitis" and gave her estrogen The tumor persisting, she was finally referred to a surgeon, who had operated upon her ten days previously He had first excised the tumor locally for biopsy It measured grossly 2 cm in diameter and was a carcinoma He had then performed a "mastectomy" through a transverse incision When her family realized what had transpired they brought her from the distant city in which she lived, to me

When I examined her the transverse incision was well healed It was obvious that only the central part of the breast had been removed Its peripheral portion remained undisturbed I could not palpate any remaining tumor The pectoral muscles had not been removed, and no axillary dissection at all had been attempted I could not palpate any enlarged axillary or supraclavicular lymph nodes Skeletal and chest x-ray films showed no evidence of metastasis

Experience has taught me that in the usual breast carcinoma of no special clinical or microscopical type it is futile to try to save the patient after this kind of inadequate operative attack The carcinoma has been implanted throughout the operative field, and any subsequent surgical attempt to get beyond it will not succeed But in this particular patient I decided to attempt it, because her carcinoma was an intraductal type of the comedo variety Our experience has shown that this form of carcinoma is not as malignant as most breast carcinomas In the radical mastectomy that I performed I carried out an unusually wide removal of skin and subcutaneous tissue A large skin graft was required to close the defect on the chest wall It took me seven and one-half hours to complete the operation

A total of 57 lymph nodes were found in the operative specimen, and three of these contained metastases

My hopes were fortunately justified The patient is well more than five years after operation She owes her cure, I believe, to the fact that her tumor was a comparatively favorable intraductal type

Circumscribed Carcinoma

A special type of breast carcinoma characterized grossly by its sharply circumscribed, soft and hemorrhagic appearance, and microscopically by broad

bands or masses of cells lying in a stroma heavily infiltrated with lymphocytes is well known to students of breast disease. It has been given a variety of names such as medullary carcinoma with lymphoid infiltration and plexiform carcinoma We prefer to call it *circumscribed carcinoma* because this term best describes its gross appearance

Incidence The circumscribed type of carcinoma is rare There were only 56, or about 3 per cent, of these tumors among more than 2000 Presbyterian Hospital breast carcinomas (1915–1950) Moore and Foote who call this lesion medullary carcinoma report that it constituted 5.2 per cent of a series of breast carcinomas that they studied

The average age of our 56 patients was 48 years, or about the same as that of our patients with carcinoma of no special type



Fig 314 A large circumscribed carcinoma of the breast, with redness of the overlying skin.

Clinical Features The average duration of symptoms in our patients with this form of breast carcinoma was 6 8 months This is somewhat shorter than the comparable figure for ordinary breast carcinoma in our data, and suggests that these solid circumscribed tumors grow more rapidly

It has been our impression that circumscribed carcinomas are often unusually large but a review of the data concerning our 56 cases did not confirm this impression The average clinical diameter of our tumors was only 5 2 cm which is approximately the same as the average diameter of ordinary breast carcinoma in our data There were only four very large tumors measuring 12 cm or more in our series The average diameter of the tumors in Moore and Foote s series was only 4 1 cm

These tumors on palpation give the impression of being well delimited from

the surrounding breast tissue, as might be expected from their grossly circumscribed character They vary in consistence but are often softer than ordinary breast carcinoma Even though they are relatively fixed in the breast tissue in which they lie, their remarkable delimitation has often betrayed the examiner into thinking them benign I have made this mistake a number of times

The skin over bulky circumscribed carcinoma is occasionally reddened, presumably as a reaction to the necrosis in these tumors As I pointed out in Chapter 24, this redness has led some clinicians into classifying the lesion as inflammatory carcinoma This is an unfortunate mistake because circumscribed carcinoma is,

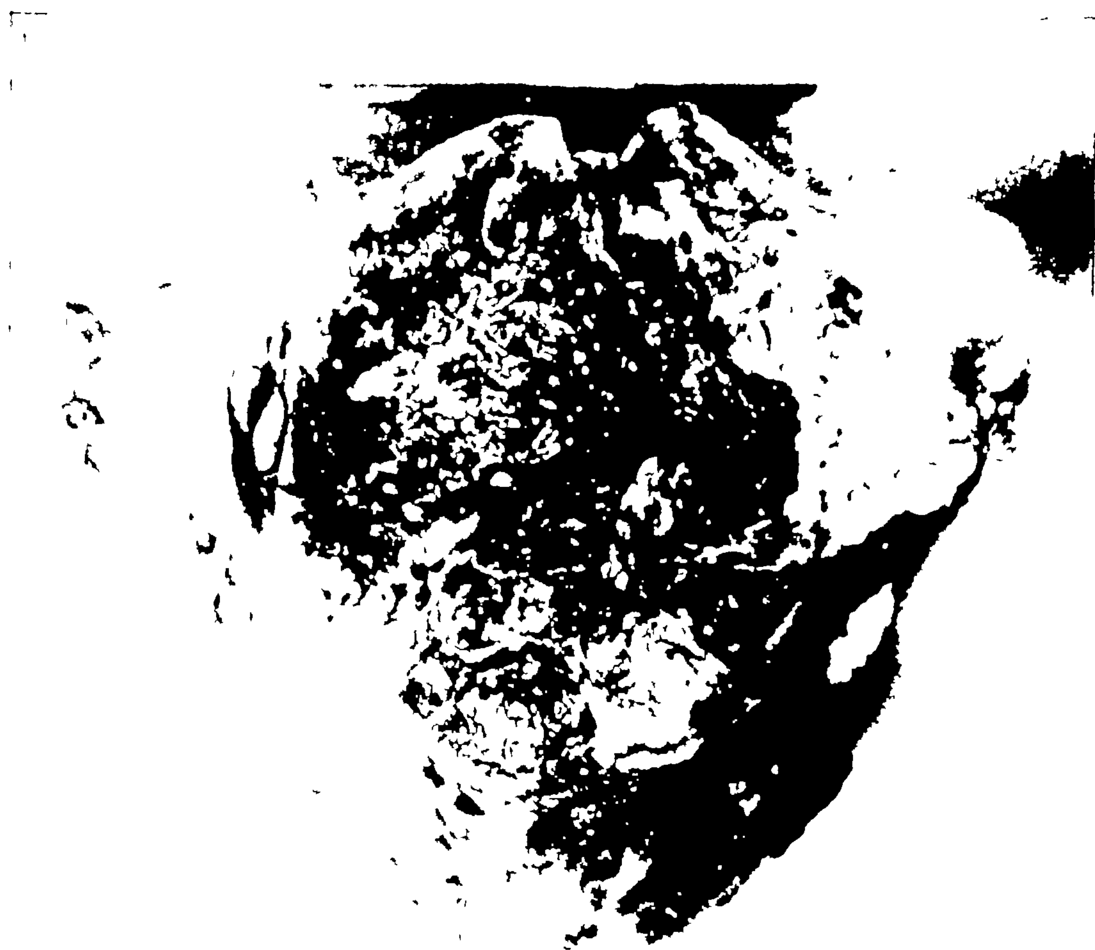


Fig 315 The gross appearance of circumscribed carcinoma

as we shall see, a very favorable type of carcinoma, best treated surgically, while inflammatory carcinoma should never be operated upon Figure 314 shows a large circumscribed carcinoma of the breast with redness of the overlying skin

Pathological Features. These tumors are often so well delimited that they give the gross impression of having a capsule (Fig 315) They do not, of course, have a true capsule, but a zone of encircling fibrosis and lymphocytic infiltration, as shown in Figure 316, gives this illusion The cut surface of the tumor is often soft When well nourished, the tumor is grayish-white These carcinomas are, however, especially prone to necrosis Their centers are often largely necrotic,

and appear hemorrhagic and partly liquefied When only a rim of viable carcinoma remains the lesion may be mistaken grossly for carcinoma within a cyst.

Microscopically the carcinoma that we class as circumscribed is composed of strands and masses of cells lying in a stroma that usually shows much degeneration It is often heavily infiltrated with lymphatics which become one of its striking features (Fig 317) In other examples of this type of carcinoma the degeneration has progressed so far that only acellular debris remains in some areas (Fig 318) In some tumors fibrosis has replaced the degenerated areas.

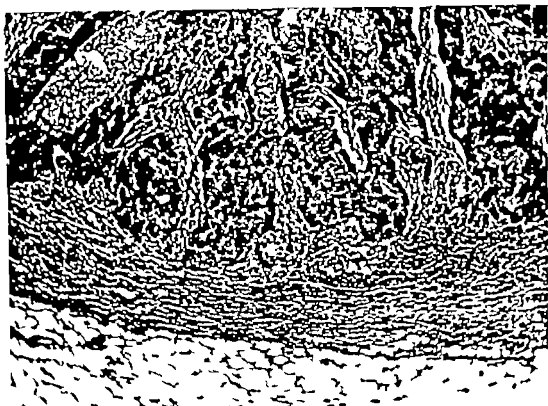


Fig 316 The zone of lymphocytic infiltration and fibrosis surrounding circumscribed carcinoma.

The tumor cells themselves lie solidly packed together without any intervening fibrillar matrix and form broad, anastomosing bands or masses of cells. The individual cells are large—in general larger than any other type of breast carcinoma. Their cytoplasms are basophilic and often show vacuoles. The nuclei are unusually large and hyperchromatic Bizarre giant and multinucleated cells are not infrequently seen (Fig 319) Mitoses are numerous Microscopically these tumors look highly anaplastic and malignant.

Treatment Radical mastectomy was done in 55 of our 56 patients with circumscribed carcinoma Only 25.5 per cent were found to have axillary metastases (Table 93) an incidence of less than one half of that of breast carcinoma of no special type in our data In Moore and Foote s series of cases of "medullary" carcinoma 42 per cent had axillary metastases

The results of operation were correspondingly good in our series of cases Two of our patients succumbed to the operation and three others died of intercurrent

Fig 317 The characteristic microscopical appearance of circumscribed carcinoma Broad bands of cells lie in a stroma containing many lymphocytes

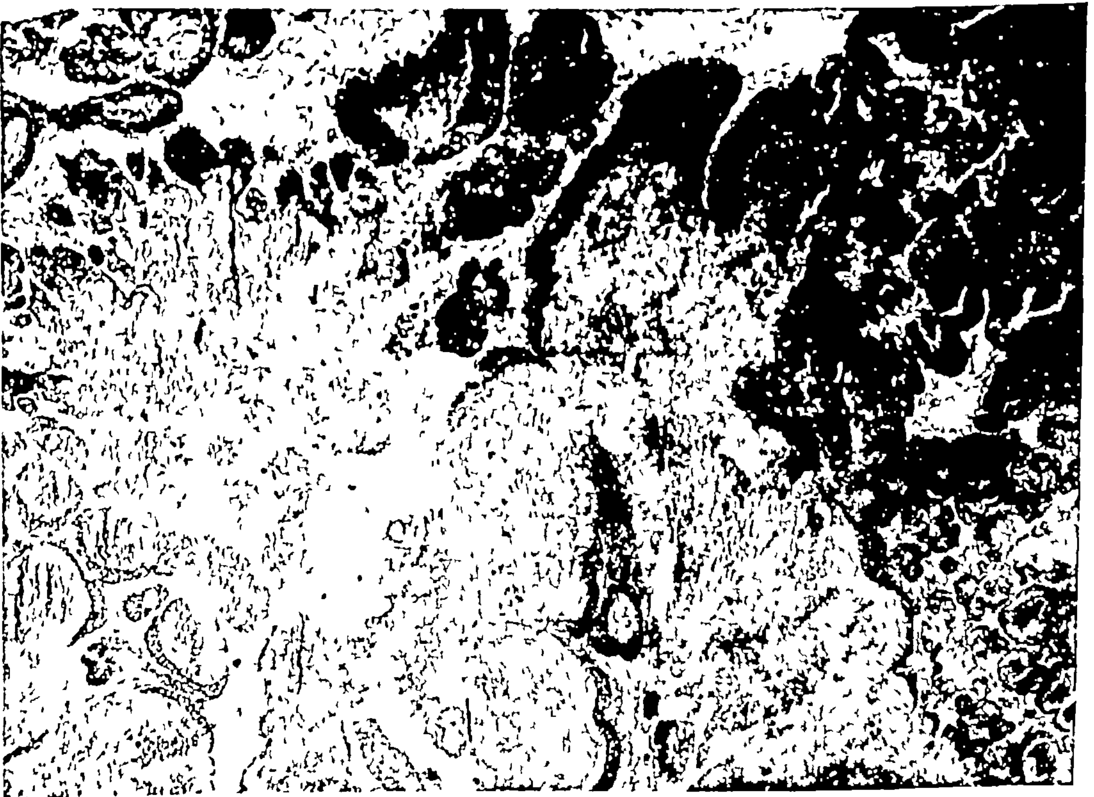


Fig 318 Advanced necrosis in circumscribed carcinoma

disease without recurrence before five years had elapsed. In studying the results of treatment in a special type of carcinoma it seems fair to subtract such cases If this is done, 31 of 50 patients treated by radical mastectomy were cured for five years Another of our patients who did not receive radical mastectomy was apparently cured by local excision followed by radiation If this last case is included, our five year clinical cure rate is 56 4 per cent In Moore and Foote s series of 52 patients with circumscribed carcinoma the results of operation were also exceptionally good

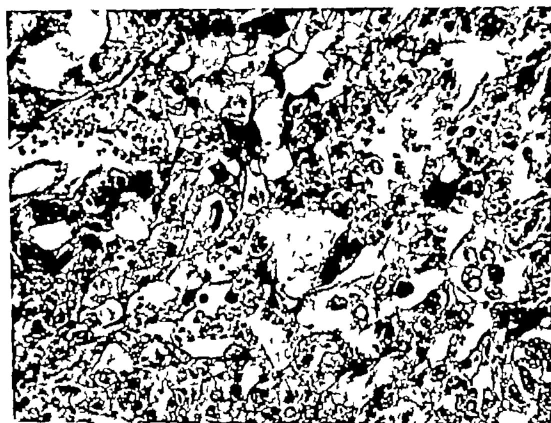


Fig. 319 Bizarre giant multinucleated cells in circumscribed carcinoma

Table 93. 55 Cases of Circumscribed Carcinoma Treated by Radical Mastectomy (Presbyterian Hospital, 1915–1950)

1 Average age	48 years
2. Average duration of symptoms	6 8 months
3 Average clinical size of tumor	5 2 cm.
4 Per cent with axillary metastases	25 5
5 Number dying within 5 years from operation or intercurrent disease—no known carcinoma	5
6. Number of 5 year clinical cures	31
7 Per cent of 5 year clinical cures	56 4

The following case illustrates the favorable character of the circumscribed type of carcinoma

Mrs A. W a housewife aged 44 was admitted to the Presbyterian Hospital with a tumor of the left breast. She had first discovered it six months previously while it was

small. It had grown steadily. One week before admission she noted spontaneous yellowish discharge from the nipple.

Examination showed the upper outer sector of the left breast to be filled by a large tumor measuring 8 cm. in diameter. It was hard, rather well delimited, but relatively fixed in the surrounding breast tissue—like a circumscribed carcinoma. In the forward bending position there was definite skin dimpling in the skin over the tumor. There was no edema of the skin. Although the palpation of the breast was gentle, the left nipple began to ooze yellowish serum during the examination. In the left axilla there was a single 1 cm., firm node that I thought contained metastasis.

Radical mastectomy with extensive sacrifice of skin, requiring a large skin graft, was performed. The tumor proved to be the circumscribed type, being grossly sharply delimited from the surrounding breast. To my surprise, there were no metastases in 17 axillary nodes.

When last seen twelve years later, the patient had no evidence of recurrence of her breast carcinoma.

My conclusions regarding circumscribed carcinoma are that although it grows rapidly, it metastasizes less often than ordinary breast carcinoma, and is correspondingly more often curable by operation.

Mucoid Carcinoma

Many carcinomas of the breast, when studied microscopically with the mucicarmine stain, will be found to contain mucin in varying amounts. Frantz studied the phenomenon and its prognostic significance. Barbieri and his associates have also carried out extensive histological investigations of mucin formation in carcinoma. The mucin is usually present in the form of intracellular droplets, but occasionally it appears in small scattered pools. We do not classify such tumors as mucoid. We limit this designation to breast carcinomas in which the mucoid change is marked, forming large lakes of mucoid material, which are often visible grossly.

We prefer the term *mucoid* rather than colloid or gelatinous, which are more commonly used, for this form of breast carcinoma. Gelatinous is a purely descriptive term. Colloid is inaccurate. Mucoid is more appropriate, because it is today generally accepted that the material that characterizes this group of breast tumors is mucin that has accumulated by secretion from malignant epithelial cells. Fifty years or more ago, when there was a considerable interest in this group of tumors, and large series of cases were collected and studied and reported in two classical papers by Lange and by Gaabe, the question of whether the mucoid material originated from the stroma or the epithelium of the tumor was hotly debated.

Incidence. True mucoid carcinoma is rare. In the largest reported case series (Lee et al., and Geschickter) this type constituted only from 1 to 3 per cent of all breast carcinomas.

In the Presbyterian Hospital between 1915 and 1942, 52 out of a total of 1544 breast carcinomas, or 2.6 per cent, were classified as mucoid.

The average age of the 46 treated patients in our series was 56 years. This is definitely older than the average age for ordinary breast carcinoma in our Presbyterian Hospital series—50 years.

Clinical Features. Most of those who have written about mucoid carcinoma have emphasized the slow growth and large size of these tumors, but critical

study of the data they have presented regarding these characteristics is not entirely convincing Some of these tumors certainly grow slowly and attain a large size, but so do some ordinary breast carcinomas

In our Presbyterian Hospital series of 46 patients with mucoid carcinoma treated by radical mastectomy the average duration of symptoms was 11.2 months, as compared with 10 7 months for all our breast carcinomas The average size of our mucoid carcinomas, by clinical measurement, was 4 7 cm or almost the same as that for our entire series of breast carcinoma

Some mucoid carcinomas, on palpation are remarkably well delimited and seem to be fluctuant On these grounds I have several times mistaken them for cysts. In our entire series of 52 cases there were 17 that were described as well delimited. Five of these were thought to be fluctuant

Halsted, in 1915 described a clinical sign that he had noted in 4 cases of mucoid carcinoma He wrote there was conveyed to the finger on testing for elasticity a peculiar sensation which in the first instance made me apprehensive lest I had ruptured a possible capsule of the nodule it might be defined as a delicate swish or crush of a jelly like structure under tension with the suggestion of a delicate bursting

Halsted s gentleness and precision were well known and it is likely that most examiners would miss what he felt I have never myself experienced this swishing or crushing sensation

Pathology Mucoid carcinoma can often be recognized grossly from its sharply delimited, seemingly encapsulated character its soft and jellylike consistence and its mucoid translucent appearance Figure 320 shows the gross appearance of one of these tumors

Microscopical study of these tumors indicates that the mucoid material is secreted by the tumor cells These cells often have acidophilic cytoplasms and tend to form acini as in Figure 321 They are lost to a varying degree in the lakes of mucoid material that they secrete In some tumors only scattered small groups of cells remain (Fig 322)

It is important for pathologists to be on guard against mistaking adenofibromas showing extensive myxoid degeneration for mucoid carcinoma. It is very difficult to make good frozen sections from both of these tumors, and the pathologist is tempted to rely on gross appearance The adenofibromas are truly encapsulated while the mucoid carcinomas do not have a real capsule The cut surface of the adenofibroma bulges, while the mucoid carcinoma does not. But the differential diagnosis should be made only on microscopical grounds

Treatment Radical mastectomy was performed in 46 of our 52 patients with the mucoid type of carcinoma. Axillary metastases were found in only 17 or 37 per cent, as compared with an incidence of axillary metastases of 66 4 per cent in breast carcinoma of no special type in our hospital

The cure rate was correspondingly good (Table 94) Twenty seven or 58 7 per cent of the patients, were well five years after operation, as compared with a five year clinical cure rate of 40 1 per cent for patients with carcinoma of no special type in our hospital

The comparatively slower growth rate of mucoid carcinoma is reflected by late recurrence following mastectomy The following case history is an example





Fig 320 The soft, jellylike, encapsulated gross appearance of mucoid carcinoma

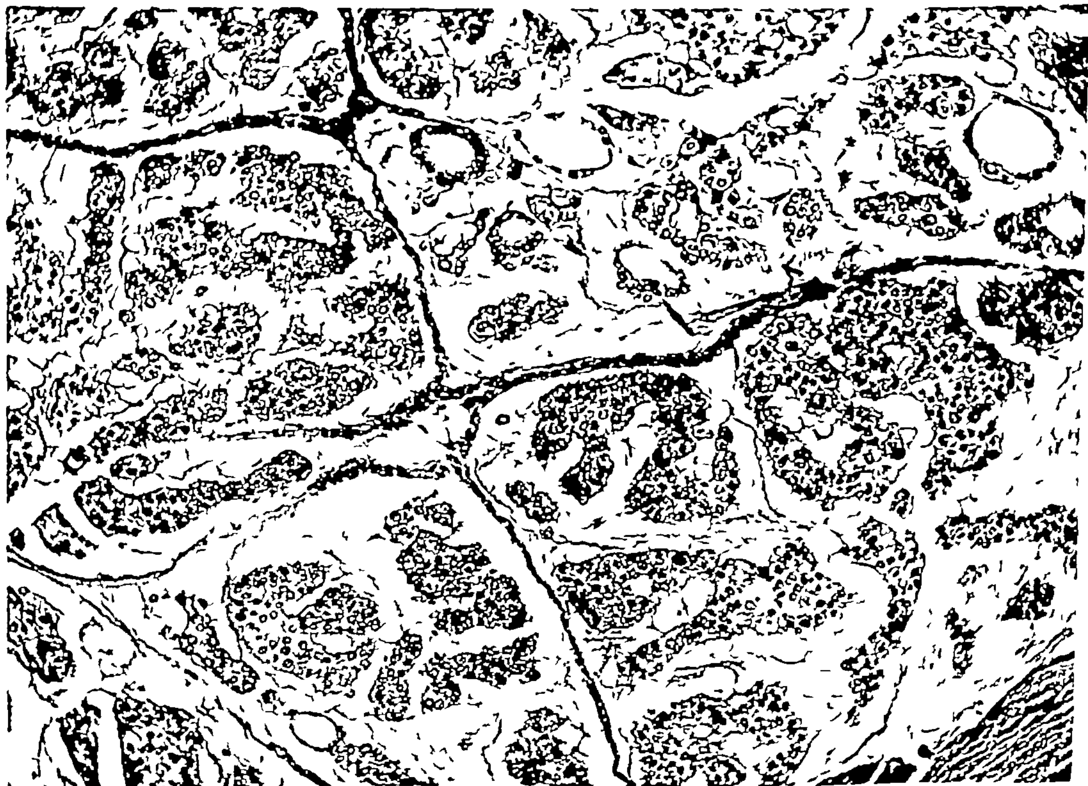


Fig 321. Characteristic microscopic appearance of mucoid carcinoma.



Fig 322. Advanced mucoid change in mucoid carcinoma.

Miss M O., aged 54 was admitted to the Presbyterian Hospital for a tumor of the left breast that she had had for two months. It was a rounded well delimited firm mass 4 cm in diameter situated in the lower central portion of the breast. Biopsy showed it to be a soft, hemorrhagic, mucoid carcinoma Radical mastectomy was done No metastases were found in the axillary nodes

The patient was well until nine years and three months later when a metastasis was removed in the right supraclavicular area. Two years later another metastasis was excised from the right scapular region The patient is at the moment without further recurrence, but she will no doubt eventually succumb to her disease.

The Apocrine Type of Breast Carcinoma

The *morphology of occasional breast carcinomas is so reminiscent of the* "apocrine" or pale epithelium of the breast that we are tempted to infer that they originate from these cells Lee and his associates, and more recently Higginson and McDonald, have written about these sweat gland carcinomas

Table 94. 46 Cases of Mucoid Carcinoma Treated by Radical Mastectomy
(Presbyterian Hospital, 1915–1950)

Average age	56 years
Average duration of symptoms	11 2 months
Average clinical size of tumor	4 7 cm
Number with axillary metastasis	17
Per cent with axillary metastasis	37 0
Number of 5 year clinical cures	27
Per cent of 5 year clinical cures	58 7

In these carcinomas the cells have the same large acidophilic *cytoplasms as the* apocrine cells of the normal breast (Fig 323) They tend to grow within ducts,



Fig 323 Apocrine carcinoma with large pale cells growing in ductlike formations

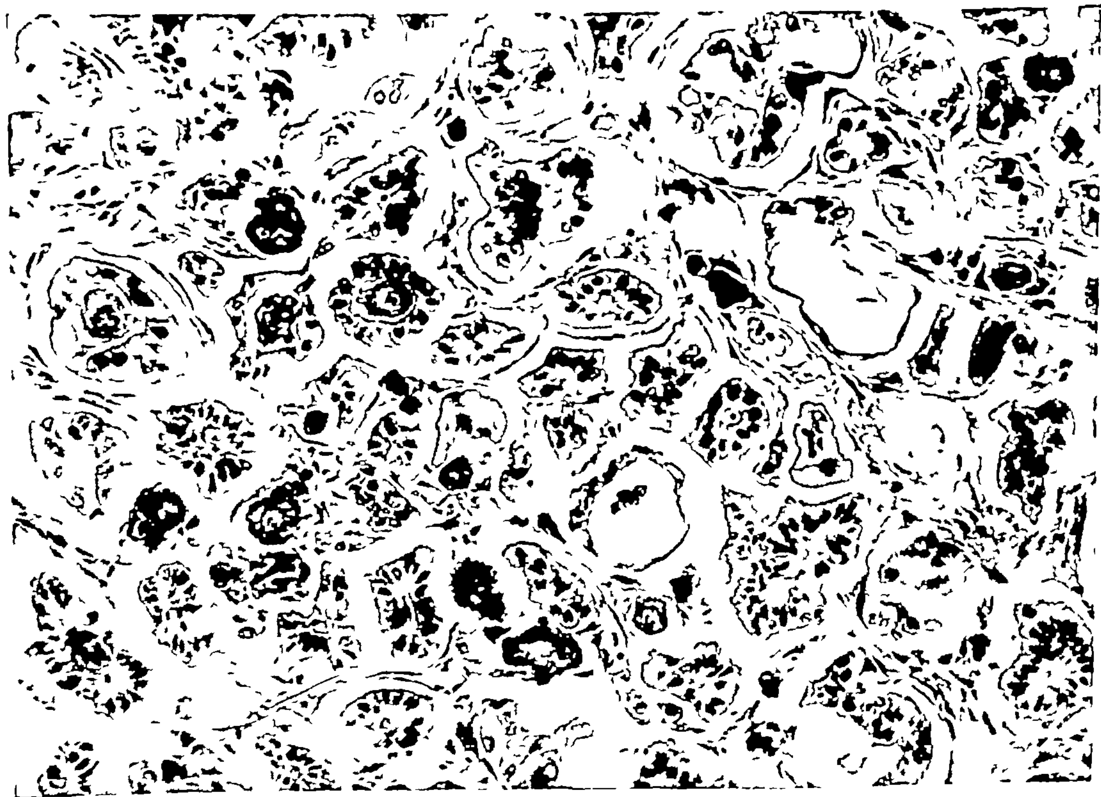


Fig 324 Apocrine carcinoma with large pale cells growing in glandular formation

forming low papillary projections In other tumors the cells form small, irregular acini (Fig 324)

There are two special features of these apocrine carcinoma cells that assist in identifying them One is the tendency of the cells to extrude their cytoplasms into the gland lumen as snouts projecting from the medial pole of the cell (Fig 325) A second feature is the presence of myofibrils in the bases of the peripheral cells in ducts. These are shown in Figure 326 in a phosphotungstic acid stain

The carcinomas that we have been willing to classify as apocrine in our laboratory have been few In reviewing ten such tumors we did not observe anything

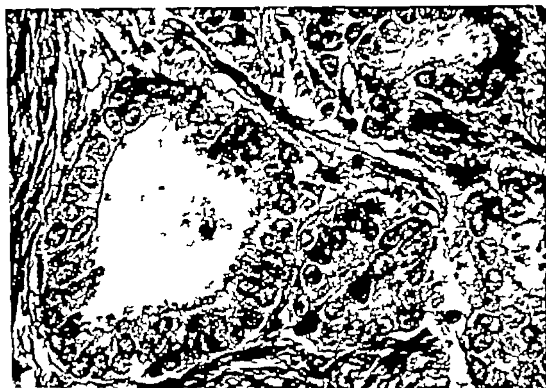


Fig 325 The cells of apocrine carcinoma extruding cytoplasm into gland lumens

particularly distinctive about their clinical character Eight of the patients were treated by radical mastectomy Only 2 of the 8 had axillary metastases One patient was lost track of but 5 of the remaining seven were well five years after operation One of these 5 developed pulmonary metastases seven years post operatively but the other 4 are well fifteen fifteen seventeen and nineteen years respectively after operation. These few cases can only suggest that the apocrine type of carcinoma is a comparatively favorable one

Carcinoma with Squamous Metaplasia

Squamous metaplasia is occasionally seen in mammary carcinomas of mice In human breast carcinoma it also occurs, as might be expected but it is rare During a thirty year period—1919–1949—only fifteen mammary carcinomas with squamous metaplasia were recorded in the Presbyterian Hospital The majority of these tumors were of the circumscribed type The squamous metaplasia oc

curred within the broad bands and masses of cells that characterize this form of breast carcinoma

In these tumors the extent of the squamous metaplasia varied greatly In some there were only scattered small areas of squamous transformation such as that shown in Figure 327, found within masses of otherwise unremarkable carcinoma

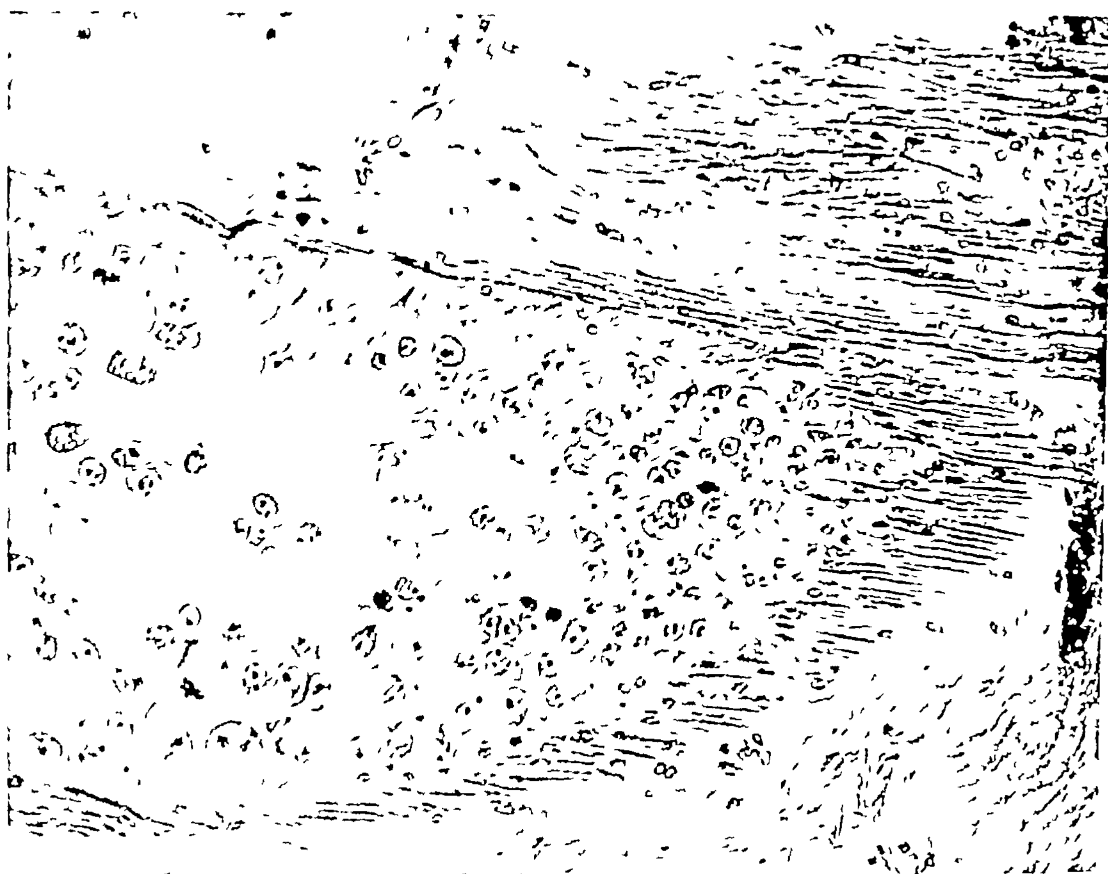


Fig 326 Myofibrils in the basal layer of cells of a duct lined by apocrine carcinoma

cells It is apparent from the study of such tumors that the squamous areas in them develop by metaplasia Even when the squamous change involves most of the tumor, and includes the development of intercellular bridges and epithelial pearls, as illustrated in Figure 328, the phenomenon is still only a metaplastic one These tumors are not pure squamous cell epitheliomas, developing as such within the breast We have no such breast tumor in our Presbyterian Hospital series of cases Stewart also stated he had none in his data

Squamous cell epithelioma developing within sebaceous cysts in the skin over the breast may grow to a large size and simulate carcinoma of the breast, which of course it is not

Good descriptions of breast carcinomas showing squamous metaplasia have been published by Loeb, by Brocq, Wolf and Giet, by Foot and Moore, by Harrington and Miller, and by Pasternack and Wirth The latter authors included in their paper an exhaustive review of previous case reports In studying the problem of histological grading in a series of breast carcinomas of the late Dr Frank Mathews I found two that showed squamous metaplasia Both tumors were highly malignant

Fig 327 A small area of squamous metaplasia in a mammary carcinoma of the circum scribed type.

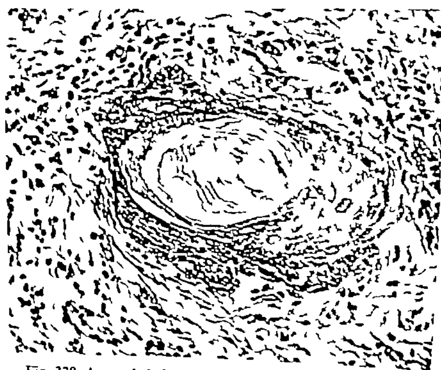


Fig. 328 An epithelial pearl formed in a mammary carcinoma.

curred within the broad bands and masses of cells that characterize this form of breast carcinoma

In these tumors the extent of the squamous metaplasia varied greatly In some there were only scattered small areas of squamous transformation such as that shown in Figure 327, found within masses of otherwise unremarkable carcinoma

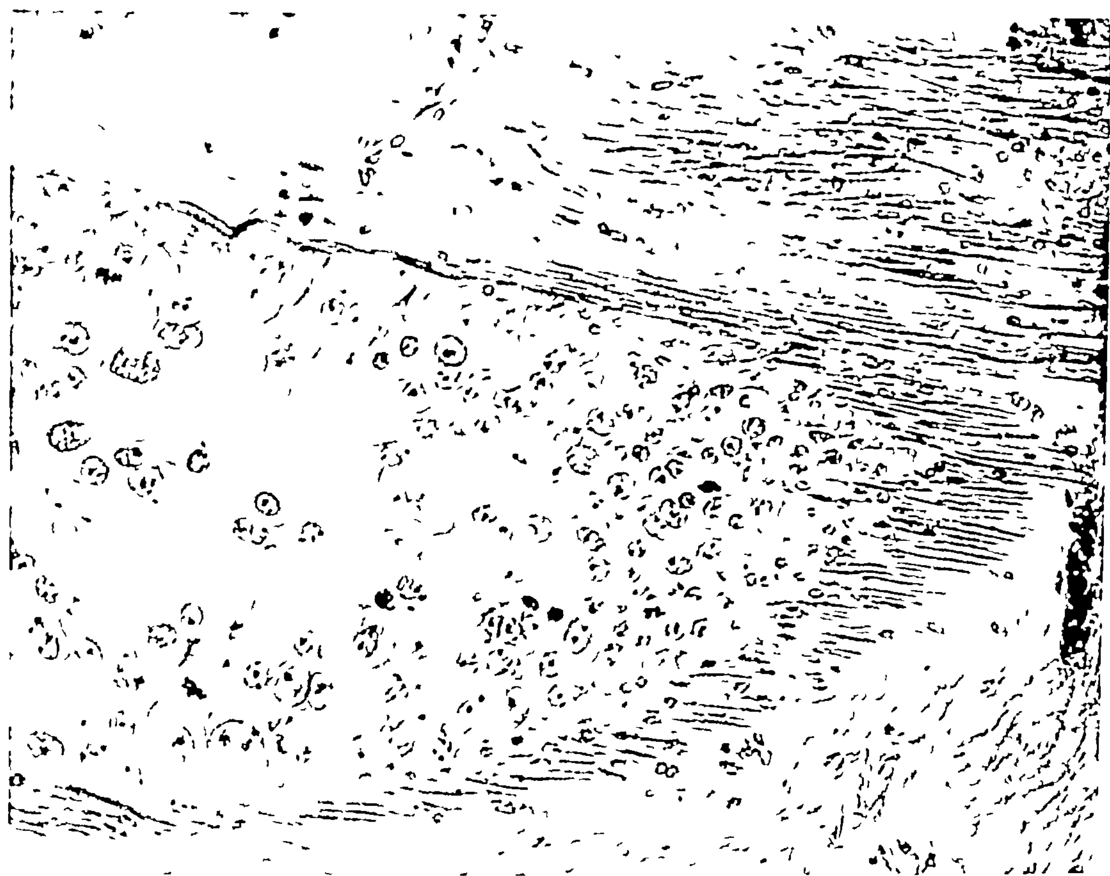


Fig 326 Myofibrils in the basal layer of cells of a duct lined by apocrine carcinoma

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In one of them there was also extensive squamous metaplasia The areas of cartilage (Fig 329) lie in masses of spindle shaped cells Between the spindle shaped cells there is a matrix of mucicarminophilic material These tumors have been called mixed tumors by some writers but it seems better to classify them as carcinomas, for no matter how predominant the embryonal cartilage may be, areas of indubitable duct carcinoma can be found in them In mammary carcinomas of the dog cartilaginous metaplasia is almost the rule. It is occasionally seen in mouse breast carcinoma. It is not unreasonable, therefore to find it now and then in human mammary carcinoma

Osseous metaplasia as shown in Figure 330 occurred in association with areas of embryonal cells of other types in one of our five cases



Fig. 330 Osseous metaplasia in mammary carcinoma

Osseous metaplasia occurring in carcinoma should not be confused with the calcium concretions the so-called psammoma bodies, that are occasionally seen in the ducts of the breasts of aged women (Fig. 331)

We do not have enough information concerning the course of the disease in our five cases to draw any conclusions regarding the degree of malignancy of these rare carcinomas

Mammary Carcinoma of No Special Type

The great majority in fact some 71 per cent, of our breast carcinomas have not been of any special microscopical type Those showing a pronounced degree of desmoplasia might be called scirrhous, while the softer and more cellular ones might be called medullary but these are broad descriptive terms that have, in our opinion, no definite significance as regards the natural history of the car

Review of our 15 Presbyterian Hospital cases of breast carcinoma showing squamous metaplasia does not reveal that these tumors have any distinctive clinical characteristics The average age of the patients was 49 The average duration of symptoms was 6 9 months, which is rather shorter than the duration in ordinary breast carcinoma, if such a small series of cases permits any conclusion The average size of these tumors by clinical measurement was 6 5 cm Axillary metastases were found microscopically in 43 per cent of the cases

One of the patients was treated by irradiation and was well when last heard from nineteen years later Two other patients, both of whom had very large

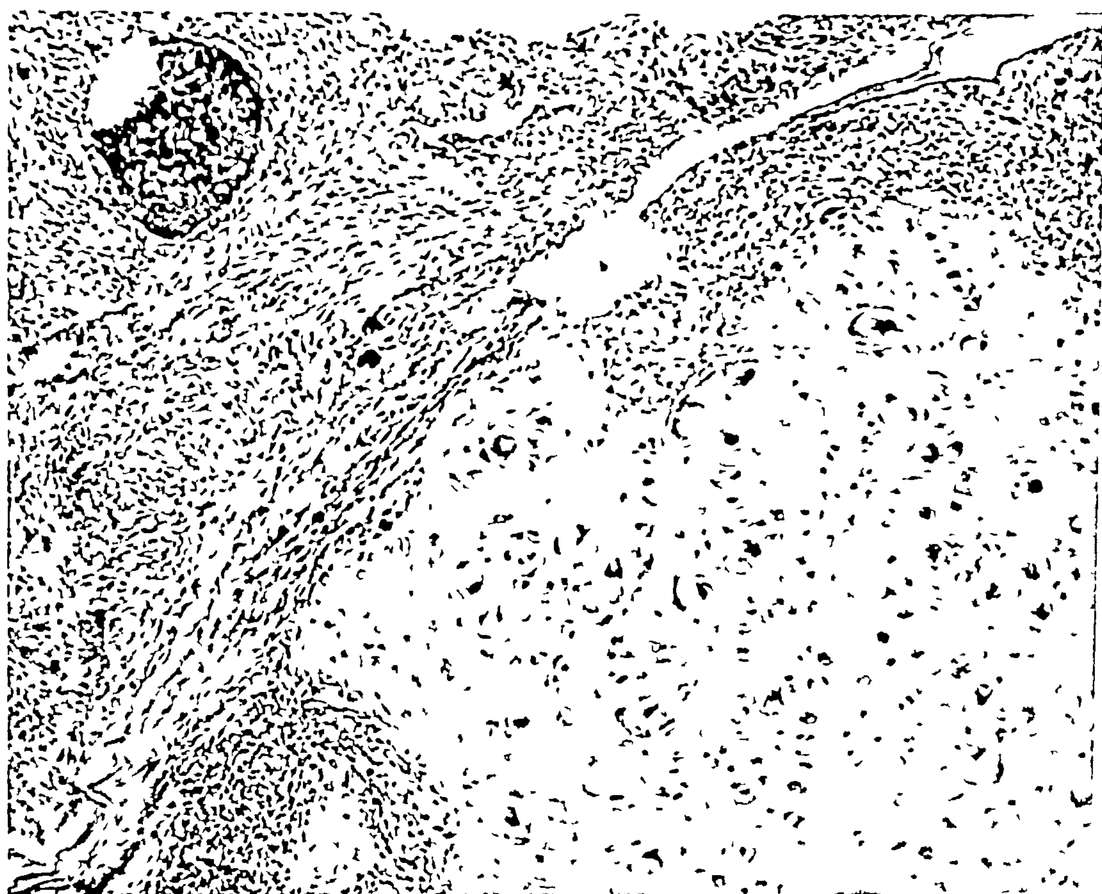


Fig 329 Cartilaginous metaplasia in mammary carcinoma

tumors and whose disease was regarded as inoperable, were treated by palliative simple mastectomy with excision of lower axillary nodes they both succumbed within a year The remaining 12 patients were treated by radical mastectomy Seven, or 58 per cent of them, were well more than five years later In 6 of these the duration of cure was ten, fourteen, fourteen, eighteen, twenty-four, and thirty-two years, respectively These carcinomas characterized by squamous metaplasia are, to judge from our Presbyterian Hospital experience, by no means as hopeless as they have sometimes been reported to be

Carcinoma with Osseous and Cartilaginous Metaplasia

Carcinomas showing cartilaginous, and particularly those showing osseous, metaplasia are the rarest breast tumors Such tumors have been well described by Biggs, and by Kreibig Five of these tumors have been studied in our laboratory

estimating the grade of anaplasia of adenocarcinoma had used loss of an adenoid arrangement of the cells, and the number of normal and atypical mitoses as his criteria. Greenough in his grading of breast carcinoma, followed Hansemann fairly closely His criteria were the arrangement of the cells around an open gland lumen, the degree of secretory activity as indicated by the presence of vacuoles and droplets of mucoid material the uniformity of size of cells and nuclei the degree of hyperchromatism of the nuclei and the number and irregularity of mitoses When tumors were graded on this basis, Greenough found a striking relationship between the grade of anaplasia and curability Sixty-eight per cent of his patients with Grade I tumors were alive five years after operation, and 33 per cent of those with Grade II tumors survived while none of those with Grade III tumors lived for five years.

Similar studies, using Greenough s method of grading breast carcinoma, were shortly carried out by White, by Lee and Stubenbord and by Smith and Bartlett. These studies in general confirmed Greenough s findings

Meanwhile, at the Mayo Clinic, MacCarty had become interested in the grading of breast carcinomas The histological characteristics that MacCarty used as a basis for grading were however quite different from those suggested by Hansemann MacCarty relied upon what he called defensive factors These included lymphocytic infiltration and fibrosis and hyalinization, as well as cellular differentiation MacCarty s pupils Flothow and Heuper applied and elaborated his method of grading breast carcinoma to case series Their follow up data were not complete and their conclusions were not convincing

French pathologists became interested in relating the morphology of breast carcinoma to its prognosis through the studies carried on by Delbet. He was particularly interested in the prognostic significance of mucin secretion He thought that the carcinomas that contained mucin were more benign. Leroux and Perrot, Moureau and Lambert, and Toro made similar studies of the significance of mucin secretion in breast carcinoma, and confirmed these findings Frantz, in our laboratory carried out a much more systematic study of the significance of mucin secretion in breast carcinoma. Although she was cautious in her conclusions, they tended to confirm the favorable prognostic significance of finding mucicarminophilic material in breast carcinomas

In 1933 I myself attempted to determine the significance of histological grading of breast carcinoma. I used for the study a remarkable series of 164 consecutive radical mastectomies performed by the late Dr Frank Mathews. The follow up was known in all but five of these patients I studied in detail the prognostic significance of fifteen different histological characteristics in the tumors of this case series Six of these characteristics were found to have a probable relationship to the degree of malignancy as expressed by the end results of treatment. These significant characteristics were similar to those which Hansemann originally proposed for the determination of grade of anaplasia They were

1 The tendency of the carcinoma to grow in a papillary character
2 An intraductal type of growth, as illustrated by comedo carcinoma.
3 An adenoid arrangement of the cells
4 Variation in size and shape of the nuclei.
5 The number of mitoses
6 The presence of mucin.

cinoma to which they are applied This brings us to the consideration of another method of classifying breast carcinomas—microscopical grading

Microscopical Grading

I have described a number of different clinical and microscopical types of mammary carcinoma and have drawn what conclusions our data seem to warrant regarding the degree of malignancy of each type Another method of determining the degree of malignancy of a tumor consists in histological grading

It was toward the end of the last century that Hansemann, in his monograph 'Studien uber die Spezificitat, den Altruismus und die Anaplasie der Zellen"



Fig 331 Calcium concretions in the breast of an aged woman

first presented the idea that a scale might be drawn up to represent the degree of anaplasia, that is, the degree to which the morphology of a tumor departs from that of the mother cells from which it arises He suggested the possibility that the degree of clinical malignancy of the tumor, as evidenced by its tendency to metastasize, might be correlated with its grade of anaplasia

Hansemann's idea was tested extensively by American pathologists in the 1920's Good evidence was accumulated that for a few special types of carcinoma, such as that in the cervix and in the rectum, the grade of anaplasia is a useful guide to the grade of malignancy

Mammary carcinoma would seem to be an ideal form of cancer upon which to test the significance of histological grading, since the disease is frequent, and abundant pathological material is secured by radical mastectomy Greenough's 1925 study of a series of cases from the Massachusetts General Hospital was the first attempt in this direction He graded the tumors in 73 cases in which complete follow-up data were available, distinguishing three grades of anaplasia which he designated as low, medium and high malignancy Hansemann himself, in

Scarff and Handley in 1938 using a system of microscopical grading rather similar to the one I worked out graded 172 breast carcinomas operated upon at the Middlesex Hospital Their findings were similar to mine and are reproduced in Table 96

Bloom has recently (1950) graded a subsequent series of Middlesex Hospital cases, using Scarff's criteria His results are shown in Table 97

Our Presbyterian Hospital 1915 to 1942 series of breast carcinomas which have been graded personally by Dr Stout show a remarkable correlation between histological grade and degree of malignancy as evidenced by the frequency of axillary metastases as well as by curability These data are shown in Table 98

Table 98. Results of Radical Mastectomy by Microscopical Grade—All Cases
(Presbyterian Hospital, 1915–1942)

Grade	Number of cases	Per cent with axillary metastases	5 year clinical cures	
			Number	Per cent
Grade I—well differentiated				
Limited to breast	52		45	86 5
With axillary metastases	32		21	65 6
Total	84	38 1	66	78 6
Grade II—moderately differentiated				
Limited to breast	165		114	69 1
With axillary metastases	257		89	34 6
Total	422	60 9	203	48 1
Grade III—undifferentiated				
Limited to breast	202		121	59 9
With axillary metastases	395		75	19 0
Total	597	66 2	196	32 8
All Grades				
Limited to breast	419		280	66 8
With axillary metastases	684		185	27 0
Total	1103	62 0	465	42 2
Unclassified	32		12	37 5
Grand total	1135		477	42 0

The factors of fibrosis and lymphocytic infiltration emphasized by MacCarty and his pupils were found to be without prognostic significance When Mathews, cases were graded on the basis of the six characteristics that I found to be significant, the correlation with five year clinical survival was as shown in Table 95

Table 95 Microscopical Grade and Survival Mathews Series of Breast Carcinomas

Grade	Number of cases	Number 5 year survival	Per cent 5 year survival	Average length of life of those dying before 5 years
1	40	32	80	3 4 years
2	66	25	38	2 3 years
3	48	6	13	1 5 years
Total	154	63	41	2 years

Table 96 Microscopical Grade and Prognosis
(Scarff and Handley)

Grade	Number of cases	Number survived 5 years	Per cent 5 year survivors	Average length of life of those dying before 5 years
1	62	27	45	3 1 years
2	66	19	29	2 8 years
3	44	10	23	2 4 years
Total	172	56	33	2 8 years

Table 97 Microscopical Grade and Prognosis
(Bloom)

Grade	Number of cases	Number of 5 year survivors	Per cent 5 year survivors
1	141	111	79
2	191	81	42
3	138	35	25
Total	470	227	48

As the years have gone by microscopical grading has therefore come to be generally accepted as a method of estimating the degree of malignancy of breast carcinoma. Many of us have some reservations regarding microscopical grading. The first is, of course, the fact that the extent of the carcinoma in the individual patient outweighs all other factors in prognostic significance. A second reservation applies to the method of microscopical grading. It should be based upon the concept of anaplasia originally suggested by Hansemann—that is, the degree to which the carcinoma departs, both in its architecture and its cytology, from the normal breast epithelium. Grading should not be based upon the so-called defensive factors—lymphocytic infiltration and fibrosis. Grading should be simplified as much as possible. Elaborate systems of grading depending upon many microscopical features and employing four or five grades are not realistic. In order to avoid emphasizing the numerical aspect of grading, Dr. Stout has preferred to use the terms *well differentiated*, *moderately differentiated* and *undifferentiated* to designate three grades only of malignancy. It is difficult to illustrate these three grades photographically because of the infinite variety of breast carcinomas. I have been content to show two extremes, a well differentiated carcinoma in Figure 332, and an undifferentiated one in Figure 333.

Some pathologists, such as Stewart, prefer to base prognosis upon the anatomical histological type of mammary carcinoma rather than upon degree of anaplasia. To him the fact that a tumor is the papillary or the circumscribed type outweighs the significance of the degree of anaplasia that its cells exhibit.

Table 99 Results of Radical Mastectomy in Special Types of Carcinoma for Patients Traced for Five Years after Treatment

(Presbyterian Hospital, 1915–1950)

Types of carcinoma	Number of cases	Estimated per cent of total group	Average age (years)	Average duration of symptoms (months)	Average clinical size of tumor (cm.)	Per cent with axillary metastases	Per cent dying less than 5 years with no evidence of cancer	Five year clinical cures: Per cent	Five year clinical cures: Standard error of percentage
Clinical types									
Papillary, 1915–1950	30	1.7	51	13.6	4.6	36.7	10.0	80.0	±7.3
Paget's disease, 1915–1949	51	3.1	50	14.4	3.0	54.9	4.0	49.0	±7.0
Inflammatory, 1915–1950	29	1.6	46	7.2	8.8	100.0	0.0	0.0	
Microscopic types									
Intraductal, excluding other special types listed, 1930–1942	102	15.0	46	7.5	4.7	64.1	2.9	57.8	±4.9
Circumscribed, 1915–1950	55	3.0	48	6.8	5.2	23.5	9.1	56.4	±6.1
Mucoid, 1915–1950	46	2.6	56	11	4.7	37.0	8.7	58.7	±7.3
Squamous metaplasia, 1915–1949	14	.7	49	6.9	6.5	42.9	0.0	57.1	±13.2
Apocrine, 1935–194[illegible]	7	1.6	48	6.9	3.2	28.6	0.0	71.4	±17.1
No special type, 1915–194[illegible]	766	70.7	50	8.3	4.9	66.4	4.7	40.1	±1.8

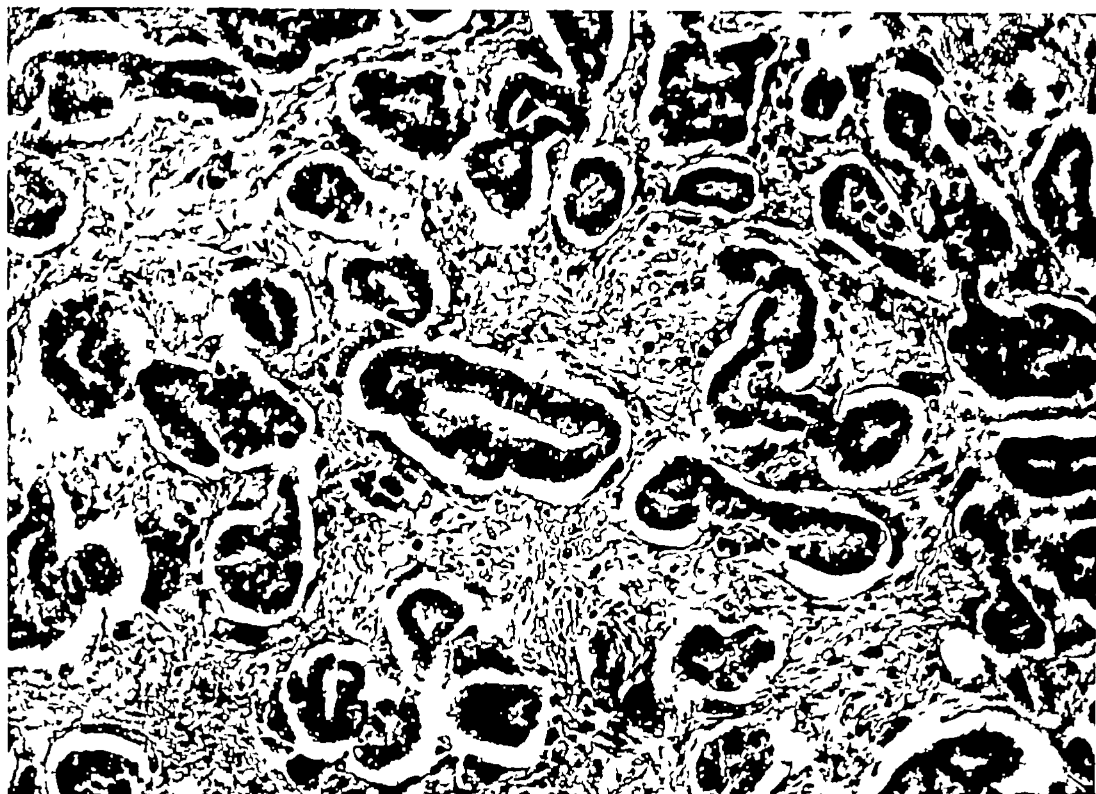


Fig 332 A well differentiated carcinoma of the breast

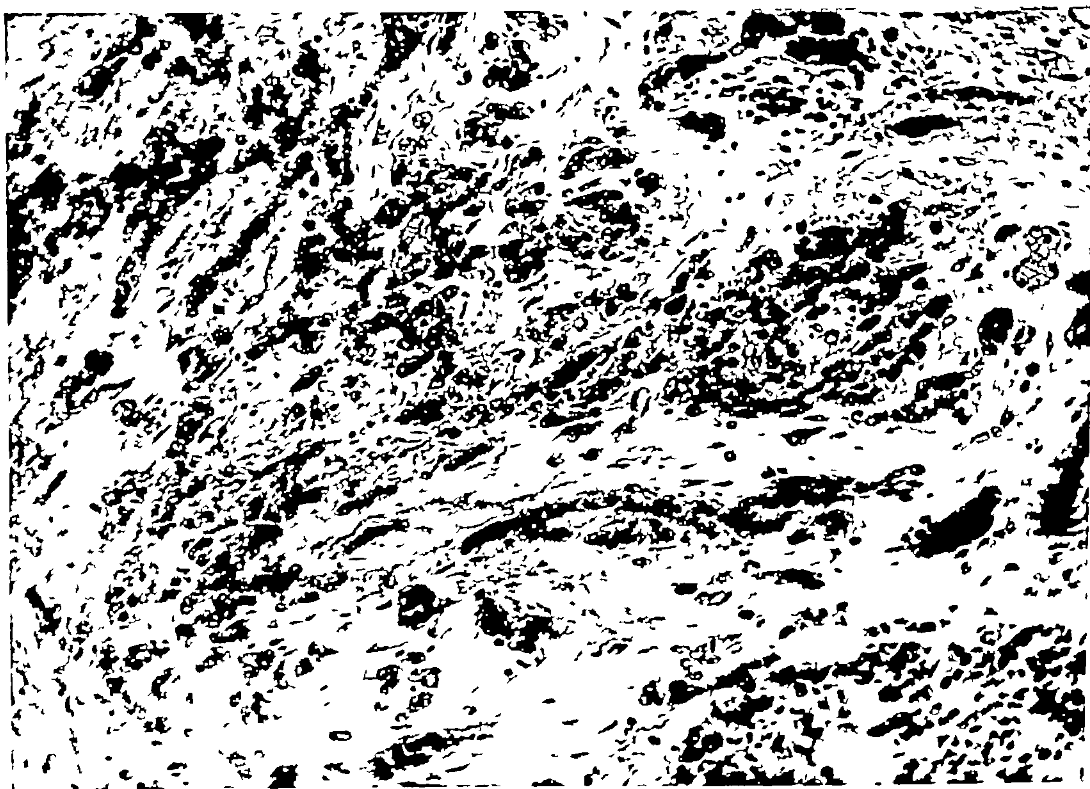


Fig 333 An undifferentiated carcinoma of the breast.

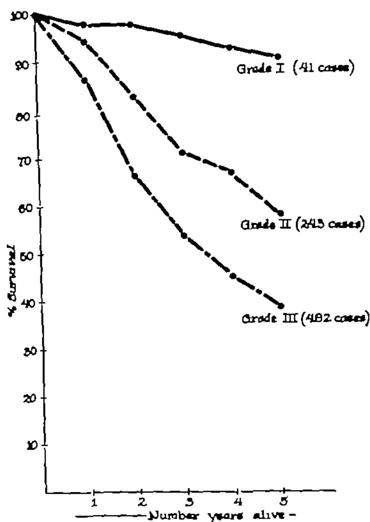


Chart 19 Survival following radical mastectomy of patients with breast carcinoma of "no special type," 766 cases—Presbyterian Hospital 1915–1942.

show a good correlation between degree of anaplasia and grade of malignancy More than four fifths of the well differentiated group were cured, and only one third of the undifferentiated group These carcinomas of no special type constituted about two-thirds of all the breast carcinomas in our data Charts 19 20 and 21 show the survival curves for breast carcinomas of no special type without and with axillary metastases

It would seem from our data that microscopical grading has a good deal of value when applied to these carcinomas that cannot be assigned to any special clinical or microscopical type Microscopical grading gives us useful information regarding the prognosis of this large group of carcinomas of no special type Pathologists like Stewart who disparage microscopical grading, give us no help in judging the prognosis of patients with these carcinomas I therefore believe that microscopical grading, used within the limitations that I have suggested has a practical value and should be continued and encouraged

Table 100 Results of Radical Mastectomy in Carcinoma of No Special Type by Microscopical Grade for Patients Traced Five Years Following Treatment

(Presbyterian Hospital, 1915–1942)

Grade	Number of cases	Estimated per cent of total group	Average age (years)	Average duration of symptoms (months)	Average clinical size of tumor (cm.)	Per cent with axillary metastases	Per cent dying in less than 5 years with no evidence of cancer	Five year clinical cures: Per cent	Five year clinical cures: Standard error of percentage
Grade I—well differentiated									
Limited to breast	21			10.5	2.6			100.0	
With axillary metastases	20			11.7	4.4			65.0	±10.7
Total	41	4.1	49	11.1	3.4	48.8	2.4	82.9	± 5.9
Grade II—moderately differentiated									
Limited to breast	89			6.0	4.0			68.5	± 4.9
With axillary metastases	154			12.8	4.8			36.4	± 3.9
Total	243	23.1	50	8.3	4.5	63.4	5.3	48.1	± 3.2
Grade III—undifferentiated									
Limited to breast	147			6.1	4.1			62.6	± 4.0
With axillary metastases	335			9.0	5.8			19.1	± 2.1
Total	482	45.2	50	8.1	5.3	69.5	4.6	32.4	± 2.1
All Grades									
Limited to breast	257			6.4	4.0		6.2	67.7	± 2.9
With axillary metastases	509			9.3	5.5		3.9	26.1	± 1.9
Total	766	72.4	50	8.3	4.9	66.4	4.7	40.1	± 1.8
5-yr clinical cures	307			7.7	4.1	43.3			
Not 5-yr clinical cures	459			8.7	5.5	81.9			

"Appropriate anatomical histological classification," Stewart writes, "obviates the need of grading."

To test the validity of this point of view with our data we have prepared tables that show the duration of symptoms, the size of the tumor, the incidence of axillary metastasis, and the results of radical mastectomy for the various special clinical and microscopical types of breast carcinoma, as well as for all other breast carcinomas of no special type in our Presbyterian Hospital series (Tables 99 and 100). These carcinomas of no special type, when graded microscopically,

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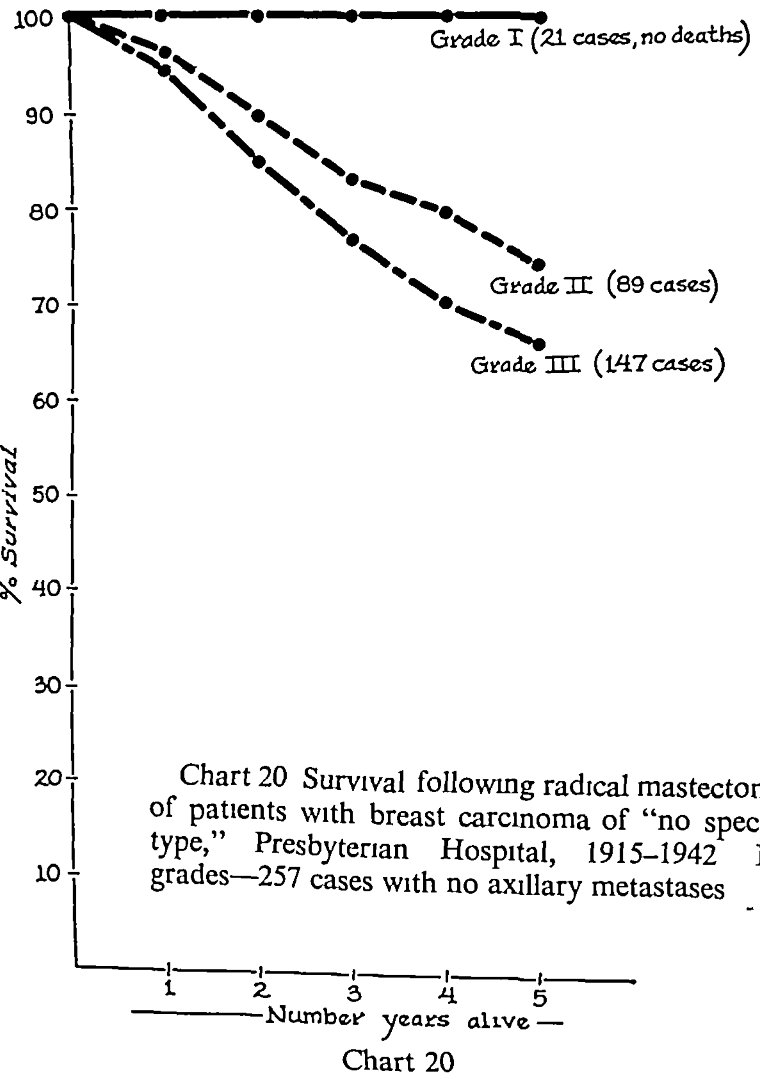


Chart 20 Survival following radical mastectomy of patients with breast carcinoma of "no special type," Presbyterian Hospital, 1915–1942 By grades—257 cases with no axillary metastases

Chart 20

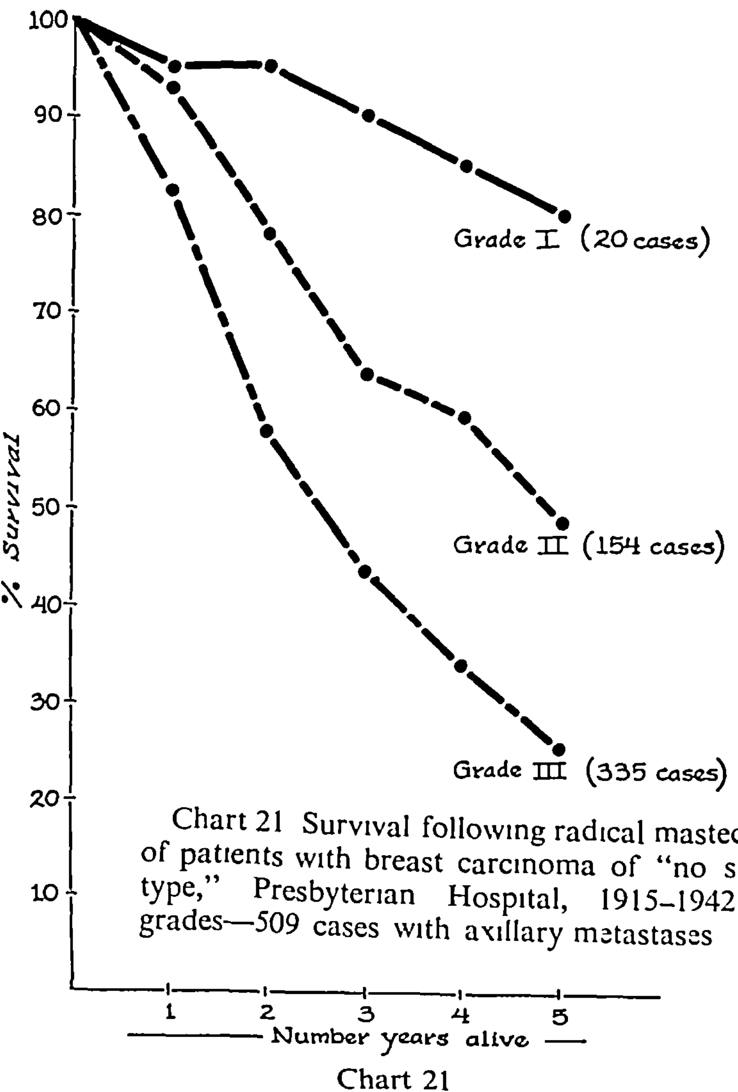


Chart 21 Survival following radical mastectomy of patients with breast carcinoma of "no special type," Presbyterian Hospital, 1915–1942 By grades—509 cases with axillary metastases

Chart 21

CHAPTER 26

THE CHOICE OF TREATMENT FOR CARCINOMA OF THE BREAST

There are only three methods of treatment for carcinoma of the breast that have a proved value They are surgical removal irradiation and finally alteration of the hormonal physiology Each of the three methods has definite limitations both as to its inherent capacity to control carcinoma and also as to the manifestations of the disease to which it can reasonably be applied Surgical removal and irradiation are both local methods of treatment It is not generally realized that modern intensive irradiation aiming at cure of primary breast carcinoma can only encompass a limited local area of tissue The hormonal attack is of course a systemic one and has an effect upon carcinoma throughout the entire body

In discussing the choice of treatment for breast carcinoma I must at the outset state what I believe to be a basic premise It is simply that the three methods of treatment—surgery irradiation, and hormonal attack —are effective in my hands in the order that I have named them. I will document this premise in discussing the results of these three methods in Chapters 27 28, and 29 devoted to a detailed discussion of each At this point I can only summarize my point of view by stating that the hormonal attack is not curative and therefore not to be considered when the disease is early enough to hope for cure In the cases in which cure is possible surgery is preferable for two basic reasons First, when the surgeon succeeds in entirely removing the carcinoma the patient is better off than when her carcinoma has been irradiated, because the surgeon s success is permanent, while irradiation can only hope to lock the carcinoma up in a fibrous prison, from which there is a considerable chance of the disease escaping after a time and growing again in all its original vigor Secondly it is my experience that a skillfully performed radical mastectomy has less morbidity than skillfully applied intensive irradiation

Each of these three methods of attacking breast carcinoma—surgery irradiation, hormones—penalizes the patient. They should never be used needlessly or futilely The choice of the best method of treatment for the individual patient is therefore a matter of very great importance

In the present chapter I will attempt to deal with the question of a choice of surgery or irradiation in the initial local attack upon primary carcinoma of the breast.

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Steinthal found that none of his Stage 3 cases were cured by operation, and he therefore advised against it. Staging originated in this way as a clinical guide to the selection of patients for surgery Staging has since been elaborated however into complex classifications used to compare the results of different methods of treatment. This is a different problem from that of the selection of patients for operation

Steinthal s staging was based, of course upon clinical features His concept was widely taken up in Germany and the Scandinavian countries in studying the results of methods of treatment. It was shortly emphasized by several of the Scandinavians in particular that clinical findings are unreliable in distinguishing Stage 1 patients (those without axillary metastases) from Stage 2 patients (those with axillary metastases but still operable) The Scandinavians substituted pathological for clinical evidence as to the presence of axillary metastases and evolved a system of staging which is still widely used It is as follows

Stage 1 Locally operable, no axillary metastases as determined by microscopic examination of all axillary nodes

Stage 2 Locally operable, with axillary metastases proved microscopically

Stage 3 Inoperable because of local extent of disease or because of distant metastases

Portmann devised a more elaborate plan for staging breast carcinomas again based on both clinical and pathological criteria. His plan follows

Group or Stage I

Skin—not involved

Tumor—localized in breast and movable

Metastases—none in axillary lymph nodes (microscopical examination) or elsewhere

Group or Stage II

Skin—not involved

Tumor—localized in breast and movable

Metastases—few axillary lymph nodes involved (microscopical examination) no other metastases.

Group or Stage III

Skin—edematous brawny red induration and inflammation not obviously due to infection extensive ulceration multiple secondary nodules

Tumor—diffusely infiltrating breast fixation of tumor or breast to chest wall edema of breast secondary tumors

Metastases—many axillary lymph nodes involved or fixed no clinical or roentgenologic evidences of distant metastases

Group or Stage IV

Skin—as in any other group or stage.

Tumor—as in any other group or stage

Metastases—axillary and supraclavicular lymph nodes extensively involved, and clinical or roentgenologic evidences of more distant metastases

This type of combined clinical and pathological staging cannot, of course, be used to select the patients suitable for operation, because Stage I can only be distinguished from Stage II after the axilla has been dissected

It is only during the last decade that irradiation has begun to compete seriously with surgery as a method of attacking primary breast carcinoma locally The results obtained by such leaders as Lenz in our own clinic, by Baclesse at the Institut Curie, Williams at St Bartholomew's, and McWhirter in Edinburgh, utilizing the modern technique of protracted irradiation, warrant serious consideration of irradiation as a primary method of treatment It is also only recently that surgeons in general have begun to be aware of the unsatisfactory results of the surgical attack upon carcinoma of the breast when surgery is used indiscriminately These two factors, the recognition of the efficacy of irradiation, and the realization of the poor results of indiscriminate surgery, have created a dilemma in the minds of many physicians as to the correct choice of primary treatment for breast carcinoma

The choice of surgery or irradiation is an exceedingly complex matter It depends not only upon which is the more successful method of treatment as measured by cure and survival rates, but upon the penalty the patient pays in morbidity, the availability of the two methods of treatment, and finally upon their financial cost I have no illusion that it is possible, in view of all these complexities, and the incompleteness of our present knowledge of breast carcinoma, to say boldly what is the best treatment for all primary breast carcinomas I do believe, however, that I can present evidence that for certain well defined types of the disease certain methods of treatment in my hands are preferable

Clinical Classification of the Extent or Stage of Breast Carcinoma

If, as I suggest, surgery is the preferred method of treatment for certain types of breast carcinoma, the first step toward its proper use is careful selection of the patients for whom it can be used with benefit A basic premise is that mastectomy should never be performed when the disease has extended beyond the operative field In addition, experience has taught us that certain types of carcinoma, even when confined to the operative field, cannot be controlled by surgery and are better treated by irradiation Dr Stout and I have called the criteria that enable us to select patients suitable for operation *criteria of operability* We might call them *criteria of curability by operation*, except that it is a longer phrase

The need of some kind of practical rule for selecting the patients who would benefit from operation was first appreciated by Steinthal In 1905, in reviewing his results at Stuttgart with breast carcinoma, he found that there were certain clinical types of the disease in which operation was futile He divided his cases into three groups or stages, as follows

"*Stage 1* Cases in which the tumor has apparently grown very slowly, is only a few centimeters in diameter, is situated entirely within the breast tissue and is not fixed to the skin, and in which there are only a few axillary nodes that are ordinarily not found until operation

"*Stage 2* Cases in which the tumor has definitely enlarged, has become adherent to the skin, and in which there are definitely palpable axillary nodes Most patients who come to operation are in this stage

"*Stage 3* Cases in which the tumor involves a great part of the breast, has involved the skin as well as the underlying tissues, and in which the supraclavicular nodes are involved"

under the leadership of Dr Denoix has drafted a Clinical Stage Classification of Malignant Tumors of the Breast. The proposed classification is so elaborate and its clinical criteria so vaguely defined that I shall not quote it.

None of the plans that had been devised for staging breast carcinoma seemed adequate to Dr Stout and me when some years ago we began to search for a method of accurately selecting the patients who would benefit from the classical radical mastectomy The methods by which criteria for staging had been arrived at seemed, to us wrong They were based upon conjecture as to what early and late operable and inoperable, breast carcinoma might be, rather than upon actual findings as to what types of cases had been cured by operation in carefully controlled case series

Dr Stout and I had been stimulated to search for criteria of operability by our experience in reviewing the results of treatment of breast carcinoma at the Presbyterian Hospital during the years 1915 to 1935 We were impressed by the frequency with which radical mastectomy had been performed upon patients with advanced disease, without any benefit. Several of the surgeons who had performed many of the mastectomies in the series held to the theory that patients should be operated upon and given their chance of cure no matter how small it might be The practical application of this point of view led them to attempt to remove very extensive breast carcinomas These attempts and their results, carefully documented in our case histories, made the Presbyterian Hospital series of cases a particularly instructive one to study from the point of view of determining just which of the various clinical signs of advanced carcinoma of the breast are truly indicative of inoperability

There are several features of the Presbyterian Hospital data concerning breast carcinoma that favored our inquiry Our unit record system, established in 1915 has been admirably developed by Miss Dorothy Kurtz, and the case records are easily available for study Because of the great interest of the late Hugh Auchincloss in breast carcinoma, the clinical descriptions of breast disease in our unit records have been exceptionally complete and have usually been supplemented by drawings and photographs Studies of the pathological material under Dr Stout's direction have been exceptionally thorough Finally our follow up system has been so efficient that we know what has happened to almost all our patients

Dr Stout and I had all these data concerning our breast carcinomas on punch cards when we undertook our study of the criteria of operability With the punch card method it was easy to determine the statistical significance as regards cure by operation of the various clinical signs of the extent of the disease The significance of combinations of the various individual clinical signs was also studied A large series of such correlations between clinical signs and the results of operation were worked out for the 1544 breast carcinomas coming to the Presbyterian Hospital between 1915 and 1942, inclusive

There are four types of evidence which are concerned in the problem of selecting patients with breast carcinoma for operation They are

1 The constitutional factors in the individual patient.

2. The local extent of carcinoma in the breast and in the tissues covering it and lying beneath it on the chest wall

In response to the need of a purely clinical method of staging breast carcinoma a classification was evolved at the Christie Hospital and Holt Radium Institute in Manchester, which has been widely adopted in England It has been called the Manchester System, and is as follows

"*Stage I* The growth is confined to the breast Involvement of the skin directly over and in continuity with the tumour does not affect staging, provided that the area involved is small in relation to the size of the breast

"*Stage II* As in Stage I, but there are palpable mobile nodes in the axilla

"*Stage III* The growth is extending beyond the corpus mammae, as shown by

(a) the skin is invaded or fixed over an area large in relation to the size of the breast or is ulcerated,

(b) the tumour is fixed to the underlying muscle or fascia

Axillary nodes may or may not be palpable, but if nodes are present they must be mobile

"*Stage IV* The growth has extended beyond the breast area as shown by

(a) fixation or matting of the axillary nodes,
(b) complete fixation of tumour to chest wall,
(c) secondaries in supraclavicular nodes,
(d) secondaries in opposite breast,
(e) secondaries in skin wide of tumour,
(f) distant metastases, e g , bone, liver, lung, etc "

Smithers and his associates at the Royal Cancer Hospital have devised a plan for staging which they believe to be an improvement over the Manchester plan Their plan follows

"*Stage I* Tumour clinically confined to the breast

No deep fixation

Skin dimpling or nipple retraction, but no skin infiltration

No significant* nodes palpable

"*Stage II* As in Stage I, except that mobile nodes of significance* are palpable in the axilla on the same side only

"*Stage III* As in Stages I and II, except that the skin in infiltrated in direct continuity with the tumor and may be ulcerated, or—the tumor is attached to the underlying fascia or muscle

(a) without significant* palpable axillary nodes,
(b) with mobile significant* palpable axillary nodes on the same side only

"*Stage IV* As in Stages I, II, and III, except that mobile significant* supraclavicular nodes are palpable on the same side, or parasternal or intercostal nodes on the same side are detected, the tumour is firmly fixed to the chest wall, there are skin nodules confined to the skin over the breast, but not in direct continuity with the primary tumour, there is extensive peau d'orange, the axillary nodes are matted together, fixed deeply, or infiltrating the skin which may be ulcerated

"*Stage V* There is evidence of distant metastases beyond the area of the breast, or the regional lymphatic drainage included in Stage IV "

At the 1954 São Paulo meeting of the International Union against Cancer a "Committee on Clinical Stage Classification and Statistics" was appointed which,

* Clinically suggestive of metastasis

Carcinoma develops so infrequently during pregnancy or lactation that no individual surgeon observes a great number of cases of this type, and their evidence is apt to be anecdotal rather than statistical In White s comprehensive review he collected reports of 746 breast carcinomas occurring during pregnancy or lactation—an incidence of 1 7 per cent. It should be pointed out that White was quite properly included in his series not only the cases in which carcinoma occurred coincidentally with pregnancy or lactation but all those in which the first symptom appeared within one year after pregnancy

Table 101 Results of Radical Mastectomy According to Quinquennial Age Groups (Presbyterian Hospital 1915–1942)

Age group	No of operations	Operative deaths No	Operative deaths Per cent	5-year local recurrence No.	5-year local recurrence Per cent	5-year clinical cures No	5-year clinical cures Per cent
Under 30	24	0		5	20 8	8	33 3
30–34	48	0		10	20 8	18	37 5
35–39	120	2	1 7	29	24 2	47	39 2
40–44	203	3	1 5	43	21 2	87	42 9
45–49	199	3	1 5	38	19 1	83	41 7
50–54	178	6	3 4	28	15 7	86	48 3
55–59	137	7	5 1	24	17 5	52	38 0
60–64	109	2	1 8	22	20 2	37	33 9
65–69	68	2	2 9	7	10 3	33	48 5
70 and over	49	4	8 2	4	8 2	28	57 1
	1135	29	2 6	210	18 5	477	42 0

Some years ago when Dr Stout and I reviewed our Presbyterian Hospital data (1915–1935) we found a total of 29 patients with breast carcinoma that had developed during pregnancy and lactation Twenty of them had been treated by radical mastectomy Although 3 survived five years, 2 of them already had had recurrence and died shortly The third developed recurrence at the end of six years and died eighteen months later Since Dr Stout and I were defining operability in terms of our Presbyterian Hospital experience, we could only conclude that breast carcinoma occurring during pregnancy or lactation was inoperable

Our criteria of operability have been much criticized but none has been so sharply attacked as that relating to carcinoma coincident with pregnancy and lactation. Several good reviews of the problem, particularly those by Cheek, White, and Lewison, have recently appeared The hard fact emerges from these reviews that the results of radical mastectomy are very poor indeed, no matter how optimistically they are presented Cheek compiled results that gave a 5 3 per cent five year cure rate. In White s collected series the five year survival rate was 13 4 per cent. In assessing these and other data comparing five year cure and "survival, it should be remembered that the survival rate is always approximately 10 per cent higher than the cure rate. In the face of these dismal surgical results the general conclusion among surgeons, nevertheless, seems to be that radical mastectomy is still the best treatment.

local anesthesia He described it as being hard not encapsulated and adherent to the overlying skin He was apparently content with his pathologist s diagnosis of "fibro-adenoma The tumor continued to grow however and the obstetrician s suspicions were finally aroused and he sent her to the Presbyterian Hospital in November 1944

Examination at that time, two years after the tumor had first been discovered revealed the left breast to be contracted and deformed as indicated in Fig 334 The *breast was solidly fixed to the chest wall* The whole central and lower portion of the breast was occupied by a hard tumor measuring 6 x 5 cm. At its lateral and caudad edge the tumor involved the skin and there was a small area of ulceration The scar of the previous operation crossed the lower part of the breast There were no clinically involved axillary nodes, and x ray films of the chest and skeleton were negative.



Fig. 334 Advanced carcinoma of breast, developing during pregnancy and ignored by obstetrician for 15 months.

The lesion was an obviously far advanced and inoperable carcinoma. A small biopsy of the ulcerated area confirmed this diagnosis. Curiously enough study of the microscopical section of the tissue removed by the obstetrician at the original operation showed only normal breast tissue. The conclusion seemed inescapable that in his "excision" under the difficulties of local anesthesia he had somehow removed only breast tissue adjacent to the tumor He was guilty not only of ignoring an obvious breast tumor for 15 months, but when he attempted to prove its nature by operation *he failed to get a piece of the carcinoma.*

The patient was treated by irradiation, which held the local lesion in check, but did not control the bone metastases in her spine which shortly appeared. She died in November 1947

The stage of the disease in our 48 patients was comparatively advanced. This is evidenced by the fact that 50 per cent were inoperable by our clinical criteria This was the most advanced group of cases in our series of breast carcinomas, excepting the inflammatory type.

Another evidence of the comparatively high degree of malignancy of car

The chief support for the proponents of surgery for carcinoma of the breast during pregnancy and lactation has been Harrington's 1937 report of the Mayo Clinic experience He reported survival rates for 92 *traced* patients Although the results were good in the small group of 14 of Harrington's patients who had no axillary metastases, the 78 patients (84 8 per cent) who had axillary metastases did very badly *Only 5 7 per cent survived five years*

At the time Dr Stout and I made our second report of the Presbyterian Hospital end results covering the years 1935–1942, we could still find no Presbyterian Hospital patient with a long term cure of breast carcinoma arising during pregnancy or lactation But we were well aware that in other clinics there were isolated cured cases, and in recognition of this fact we no longer included pregnancy or lactation among our contraindications to operation

We have now again reviewed our Presbyterian Hospital experience with carcinoma of the breast occurring during pregnancy or lactation Between 1915 and

Table 102 Carcinoma of the Breast Developing During Pregnancy or Lactation or Within 12 Months after the Termination of Pregnancy

(Presbyterian Hospital, 1915–1950)

Number of cases	48
Average age	34
Average duration of symptoms before admission	12 9 months
Those with inoperable disease according to our clinical criteria	24, or 50%
Total duration of disease from first symptom to death in 37 patients dying within 5 years	34 8 months

1950, 48 such primary cases came to the Presbyterian Hospital There are several features of this group of patients that are worth noting (Table 102) The average age of our patients was 34 years This agrees with an average age of 34 8 years in White's large collected series Since these patients are in the child-bearing age they can be expected to be younger than other patients with breast carcinoma

The average duration of symptoms in our series of patients when they came for admission was 12 9 months, which is about 4 months longer than for our series of breast carcinomas as a whole The reason why these women with carcinoma developing during pregnancy and lactation delay longer in coming for treatment is unquestionably that the patients themselves, as well as the physicians they consult, usually assume that the breast tumor is an abscess or some other non-neoplastic lesion associated with the pregnancy

The following is a typical story

M B , a housewife aged 40, who had had one previous pregnancy, became pregnant for the second time in November, 1942 Six months later she discovered a small hard tumor below the nipple of her left breast She consulted her obstetrician about it and he advised her to ignore it She was delivered in July, 1943, and nursed the baby until November, 1943 During all this time the breast tumor continued to enlarge slowly but gave her no pain Her obstetrician continued to ignore it

In March, 1944, the tumor began to pain her and her obstetrician decided to operate In his description of his operation he wrote that he had "excised" the tumor under

are shown in Table 104 In 24 of these patients the disease was operable according to our clinical criteria Seven developed local recurrence and 14 succumbed to their disease before five years but 10 were still well after five years These are recent cases and it cannot be said that their cure is definitive. Yet this is an astonishing result in comparison with our previous complete failure in the Presbyterian Hospital with carcinoma of the breast developing during pregnancy or lactation These results are all the more remarkable when it is seen that the incidence of axillary metastases in our patients was as high (80 6 per cent) as it usually is in pregnant or lactating patients with carcinoma.

The explanation of our success with these recent cases of carcinoma developing during pregnancy or lactation is to be found I believe in a study of the microscopical types of the carcinomas. They are classified both as to special microscopical type and grade of malignancy in Table 105 All the cured carcinomas

Table 105. Microscopical Character of Carcinoma of Breast Developing During Pregnancy or Lactation
(Presbyterian Hospital, 1915–1950)

	No. of cases	Local recurrence	5-year clinical cures
A Microscopically Favorable Cases			
Circumscribed	4	0	3
Intraductal	4	0	3
Paget s carcinoma	2	1	0
Grade I—No special type	2	0	2
Grade II—No special type	3	0	2
B Microscopically Unfavorable Cases			
Grade III	16	6	0
Total	31	7	10, or 32 /

were favorable types As I have pointed out in Chapter 25 the results of treatment for breast carcinoma in general are better in these favorable types. It is interesting to see that even in carcinoma developing during pregnancy or lactation the microscopical character of the neoplasm is still the dominant factor in determining the result of treatment.

This recent experience of ours in the Presbyterian Hospital with carcinoma occurring during pregnancy or lactation encourages us to operate upon the disease if it is operable according to our criteria of operability and particularly if the carcinoma happens to be a favorable microscopical type I cannot report however that we have as yet cured a single patient with a Grade III carcinoma developing during pregnancy or lactation.

2 *The Local Extent of Breast Carcinoma Related to Operability* In the search for more exact criteria of operability that Dr Stout and I made in our 1915–1942 Presbyterian Hospital data—a search culminating in the list of criteria of operability that we published in 1943—our chief emphasis was upon

cinoma developing during pregnancy or lactation was the short total duration of disease in these patients The average total duration from onset to death in our 37 pregnant or lactating patients who succumbed within five years was 34 8 months This figure may be compared with the average total duration of disease of 33 *months in our entire group of 120 Presbyterian Hospital patients with* breast carcinoma whom we classified as inoperable by our clinical criteria but who were nevertheless treated, all unsuccessfully, by radical mastectomy

The treatment of our 48 pregnant or lactating patients is shown in Table 103 In 11 of them their disease was so advanced that there was no question of operation, and treatment was entirely by irradiation all succumbed after an average total duration of disease of 30 1 months

Table 103 Treatment of Carcinoma of the Breast Developing during Pregnancy or Lactation or within 12 Months after the Termination of Pregnancy
(Presbyterian Hospital, 1915–1950)

Treatment	No of cases	5-year clinical cures
Radical mastectomy	31	10
Simple mastectomy	1	0
Irradiation	13	1
No treatment	3	0
Total	48	11

Table 104. Results of Radical Mastectomy in 31 Carcinomas of the Breast Developing During Pregnancy or Lactation
(Presbyterian Hospital, 1915–1950)

	No of cases	5-year local recurrence	5-year clinical cures
A Operable according to our clinical criteria	24	3	10
B Inoperable according to our clinical criteria	7	4	0
C Without axillary metastases	6	0	5
D With axillary metastases	25	3	5
Total	31	7	10, or 32%

One patient whose disease was operable refused surgery and was treated by irradiation She died 26 months after onset of her disease Another patient had a large circumscribed carcinoma Although her disease was operable according to our criteria, it was decided to treat her with irradiation That was nine years ago, and she has had no recurrence

One patient was treated by simple mastectomy and succumbed after 50 months

Thirty-one of our patients were treated by radical mastectomy The results

the criteria related to the local extent of the carcinoma The significance of each of the various clinical features of the local growth of breast carcinoma was considered separately in relation to the possibility of cure by radical mastectomy

In our study we were at once struck by the fact that there were three local clinical features which, if present, always doomed the patient These were (1) extensive edema of the skin over the breast, (2) satellite tumor nodules in the skin, and (3) the inflammatory type of carcinoma There is no need for me to describe these three clinical features at this point I have described edema of the skin over the breast and satellite skin nodules in Chapter 19 dealing with the natural history of breast carcinoma, and I have dealt with the inflammatory type of carcinoma separately in Chapter 24

Table 106 *Results of Radical Mastectomy in Categorically Inoperable Groups of Cases*
(Presbyterian Hospital, 1915–1942)

Clinical group		No of cases	5-yr local recurrence		5-yr clinical cure
			No	Per cent	No of cases
I Patients with local signs indicating categorical inoperability	Extensive edema of skin over breast	51	31	60 8	0
	Satellite nodules in skin over breast	7	4	57 1	0
	Inflammatory type of carcinoma	25	15	60 0	0
	Patients concerned	59	35	59 3	0
II Patients with distant or regional node metastasis indicating categorical inoperability	Distant metastasis	10	2	20 0	0
	Regional parasternal or supraclavicular node metastasis	16	9	56 2	0
	Edema of arm	4	2	50 0	0
	Patients concerned	29	12	41 4	0
Total of patients concerned		77	41	53 2	0

All our Presbyterian Hospital attempts at surgery for patients with any one of these three local clinical features have been disastrous There were in our data a total of 59 patients (Table 106) in whom one or more of these three clinical features were present, and for whom radical mastectomy was done Approximately 60 per cent of them had local recurrence in the operative field, and not a single one was well five years after operation It is this experience which led us to classify patients with these three local features as *categorically inoperable*

Our search in the Presbyterian Hospital data for *categorically inoperable*

clinical types of carcinoma also led us, of course, to those groups of cases in which the disease had metastasized beyond the reach of the surgeon There were three of these clinical groups

(1) Those with distant metastases
(2) Those with parasternal or supraclavicular metastases
(3) Those with edema of the arm

The futility of radical mastectomy when *distant metastases* are present needs no comment

A parasternal mass in a patient with breast carcinoma means metastasis to an internal mammary node that has grown outward and involved the overlying tissues This kind of advanced internal mammary metastasis is not curable by chest wall resection We have done the operation for several patients with such clinically evident parasternal metastases—always unsuccessfully Irradiation is a better method of treatment

Patients with *supraclavicular metastases* that are clinically evident are likewise incurable by surgery in our experience Approximately 4 per cent of our patients coming for treatment with primary breast carcinoma have had palpable supra clavicular metastases Neither surgical nor irradiation attack upon clinically evident supraclavicular metastases has saved our patients Twelve of them had supraclavicular dissection—all futilely Eggers and his associates reported a similar experience

From what we know today concerning the sequence of metastatic involvement of the regional lymph node barrier in carcinoma of the breast we must of course expect that conventional radical mastectomy will fail to cure patients with clinically evident supraclavicular metastases The supraclavicular nodes are in volved only after the nodes at the apex of the axilla or those of the internal mam mary chain have become involved. The first supraclavicular node or nodes to be involved are the sentinel node or nodes lying deep in the base of the neck upon the confluence of the internal jugular and subclavian veins. This node is not palpable clinically until metastases in it have enlarged it greatly and have ex tended in a retrograde manner to more superficially and more laterally situated supraclavicular nodes. By then the supraclavicular metastases are advanced and incurable by surgery

The usefulness of prophylactic supraclavicular dissection as practiced long ago by Halsted and more recently by Dahl Iversen is an entirely different question I will discuss it separately in Chapter 27

Edema of the arm develops in an untreated patient with carcinoma of the breast only when axillary metastases have progressed to the stage in which they partially block the lymphatic pathways through the axilla. A patient with such extensive axillary metastases cannot be cured by surgery It was attempted in four such patients in our Presbyterian Hospital series of cases and failed in all

There were 29 patients in our Presbyterian Hospital series of cases with distant or regional lymph node metastases beyond the reach of the surgeon or with edema of the arm who were nevertheless treated by radical mastectomy (Table 106) Forty-one per cent had local recurrence and none was cured

The total number of our patients falling into the clinical groups which Dr Stout and I called *categorically inoperable* because not a single patient was cured

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Our search in the Presbyterian Hospital data for *categorically inoperable*

general They did not, however present their actual cure rates for tumors of the outer sectors of the breast, and they did not define their criteria for classification as to site in detail Their data are therefore not very helpful

For the purpose of investigating the relationship of site to surgical curability in our Presbyterian Hospital data I have studied my series of 356 personal cases treated by radical mastectomy between 1935 and 1950 Our previously published 1915 to 1942 Presbyterian Hospital series of cases has the same disadvantage as the data from other hospitals quoted above namely that the site of the carcinoma

Table 107 Results of Radical Mastectomy by Site of Carcinoma; Personal Series
(Presbyterian Hospital, 1935–1950)

Site of tumor		No. of cases	5-yr local recurrence		5-yr clinical cure	
			No	Per cent	No.	Per cent
Area	*Zone*					
U Outer	A	157	19	12 1	92	58 6
L. Outer	B	34	6	17 6	15	44 1
L. Inner	C	14	4	28 6	7	50 0
L. Paraster	D	9	3	33 3	3	33 3
U Paraster	E	10	2	20 0	8	80 0
U Inner	F	40	2	5 0	29	72 5
Center	G	90	18	20 0	47	52 4
Diffuse		1	—	—	—	0 0
Indeterminate		1	—	—	1	100 0
Total		356	54	15 2	202	56 7

was recorded as a written description and not in a sketch of the breast. In my personal cases I have always made a sketch of the breast, from which the site of the carcinoma can be accurately determined Figure 335 shows the five year clinical cure rate for carcinomas in the seven different specific breast sites which I described in Chapter 4 The numbers of carcinomas in each of the different sites, the local recurrence rate, as well as the five year clinical cure rate, are shown in Table 107

The striking thing in these data from my personal cases is that carcinomas in the lower parasternal area, zone D have given the highest local recurrence rate and the lowest five year clinical cure rate. Carcinomas of the upper parasternal area, zone E, in contrast, gave comparatively good results The lateral limit of these parasternal zones, I might point out again, is 3 cm from the sternal edge and when any portion of a tumor lies medial to this line it is counted as para sternal.

by radical mastectomy, was 77 (Table 106) In studying the significance, in terms of cure by surgery, of the various clinical signs of the local extent of carcinoma of the breast in our data, it seemed necessary to exclude these 77 categorically inoperable cases, lest their presence distort our interpretation of the significance of less critical clinical features In the separate consideration of the significance of the several clinical signs of the local extent of the disease to which I now turn, the *categorically inoperable* cases have been excluded

The Site of the Carcinoma in the Breast Related to Operability One of the local features of carcinoma of the breast that has an interesting relationship to the degree of success of surgical treatment is its site in the breast

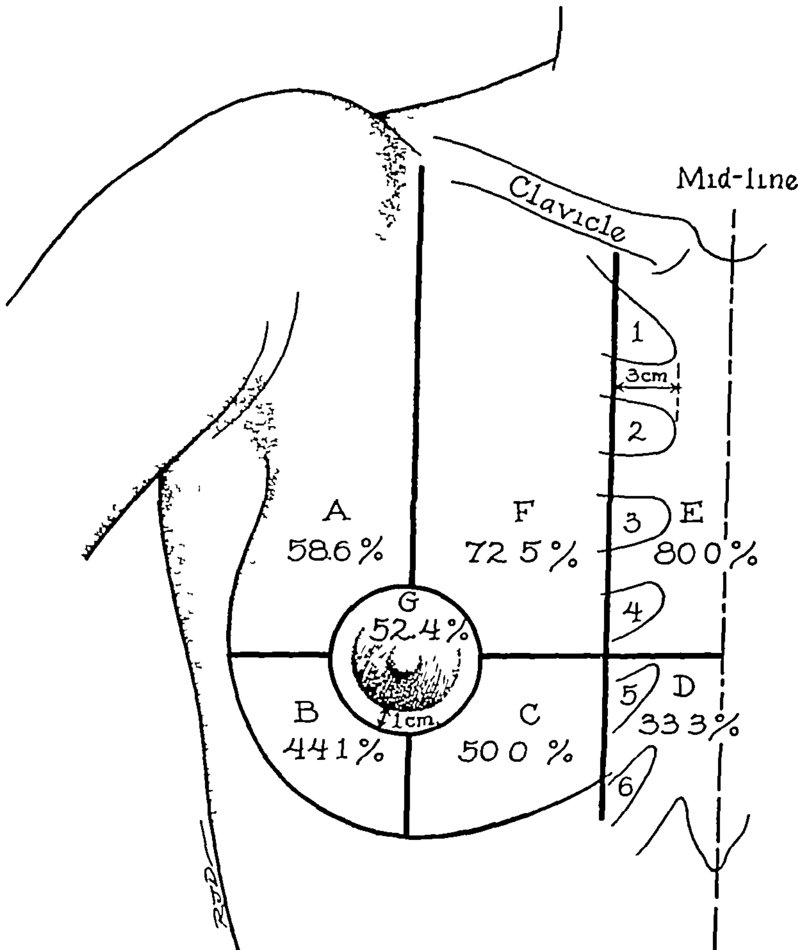


Fig 335 The clinical cure rates for carcinoma of the different sectors of the breast

Very few data as to the significance of the site of the carcinoma have been published from other clinics Smithers did not find any statistically significant differences in the survival rates for carcinoma of the different sectors of the breast in the Royal Cancer Hospital data Truscott reported that the five year survival rate in the Middlesex Hospital data was slightly lower for lower inner sector carcinomas Nohrman found that in the Radiumhemmet data Stage I carcinomas of the medial portion of the breast had a definitely poorer prognosis than Stage I carcinomas situated elsewhere in the breast Urban and Baker, reviewing the Memorial Hospital data, found that carcinoma of the central and medial areas of the breast gave somewhat lower cure rates than their breast carcinomas in

general They did not however present their actual cure rates for tumors of the outer sectors of the breast and they did not define their criteria for classification as to site in detail Their data are therefore not very helpful

For the purpose of investigating the relationship of site to surgical curability in our Presbyterian Hospital data I have studied my series of 356 personal cases treated by radical mastectomy between 1935 and 1950 Our previously published 1915 to 1942 Presbyterian Hospital series of cases has the same disadvantage as the data from other hospitals quoted above namely that the site of the carcinoma

Table 107 Results of Radical Mastectomy by Site of Carcinoma; Personal Series (Presbyterian Hospital, 1935–1950)

Site of tumor		No. of cases	5-yr local recurrence		5-yr clinical cure	
			No	Per cent	No	Per cent
Area U Outer	*Zone* A	157	19	12 1	92	58 6
L. Outer	B	34	6	17 6	15	44 1
L. Inner	C	14	4	28 6	7	50 0
L. Paraster	D	9	3	33 3	3	33 3
U Paraster	E	10	2	20 0	8	80 0
U Inner	F	40	2	5 0	29	72 5
Center	G	90	18	20 0	47	52 4
Diffuse		1	—	—	—	0 0
Indeterminate		1	—	—	1	100 0
Total		356	54	15 2	202	56 7

was recorded as a written description and not in a sketch of the breast. In my personal cases I have always made a sketch of the breast, from which the site of the carcinoma can be accurately determined. Figure 335 shows the five year clinical cure rate for carcinomas in the seven different specific breast sites which I described in Chapter 4 The numbers of carcinomas in each of the different sites, the local recurrence rate, as well as the five year clinical cure rate, are shown in Table 107

The striking thing in these data from my personal cases is that carcinomas *in* the lower parasternal area zone D have given the highest local recurrence rate and the lowest five year clinical cure rate. Carcinomas of the upper parasternal area, zone E, in contrast, gave comparatively good results The lateral limit of these parasternal zones I might point out again, is 3 cm. from the sternal edge, and when any portion of a tumor lies medial to this line it is counted as para sternal.

It is interesting to find in my data that carcinoma of the lower inner zone of the breast, zone C, situated lateral to the lower parasternal zone, gave results that were not significantly different from those for carcinoma in the breast as a whole Carcinomas of the upper inner zone, zone F, also situated lateral to the parasternal zone, gave results that were among the best in my data The number of carcinomas situated in sites C, D, and E is small, but I am tempted to conclude that the bad reputation of carcinomas of the "inner sectors" of the breast, as they are usually referred to in the published reports, is due largely to the fact that carcinomas of the lower parasternal zone give such bad results If other students of the disease will classify their carcinomas accurately as to site, following a plan such as I have used, they may find, as I do, that carcinomas of the other zones in the inner half of the breast give comparatively good results

In my data it is also true that carcinomas of the central zone of the breast, zone G, give results which are not significantly different from those for carcinoma of the breast as a whole

Table 108 Results of Radical Mastectomy in Carcinomas 10 cm or More in Diameter (Clinical Measurements)—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I Total patients Radical mastectomy	1058	169	16	477	45 1
II Tumor 10 cm or more, no other signs of locally advanced disease	26	3	11 5	11	42 3
III Tumor 10 cm or more with any one of 5 grave signs of locally advanced disease	14	3	21 4	3	21 4

The good results with carcinomas of the upper parasternal zone, zone E, and the upper inner zone, zone F, as compared with the results with carcinomas of the lower parasternal zone, zone D, suggest that some factor other than that of proximity to the internal mammary lymphatic route is concerned It may be the proximity of carcinoma of the lower parasternal zone to the lymphatic route to the liver

The Size of the Carcinoma Related to Operability Clinical measurements of the primary tumor, as well as measurements of the carcinoma as seen in the operative specimen in centimeters, are included in our data It was therefore possible for us to sort out the exceptionally large carcinomas in our data and to study their curability by operation Table 108 shows these data

In our data there were 26 patients (Class II, Table 108) in whom the only local clinical feature indicating advanced disease was the *large size* of their carcinomas

Operation was surprisingly successful in these patients, the results being approximately as good as in our series of radical mastectomies as a whole

When large size was accompanied by any single one of five other signs of locally advanced carcinoma (Class III Table 108) the results of operation were quite different The local recurrence rate doubled and the cure rate was cut in half These five other signs of locally advanced disease are ones which in our data have been found to have a very grave prognostic significance *(1) ulceration of the skin (2) edema of the skin of limited extent (3) solid fixation of the breast tumor to the chest wall (4) axillary lymph nodes measuring 2 5 cm or more in transverse diameter* and *(5) fixation of the axillary nodes to the chest wall or overlying skin*

Table 109 Results of Radical Mastectomy in Multiple Carcinoma in One Breast—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No. of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I. Total patients Radical mastectomy	1058	169	16	477	45 1
II Multiple carcinoma in one breast	27	7	25 9	14	51 9
III Multiple carcinoma in one breast *with* any one of 5 grave signs of locally advanced disease	4	1	25	0	

Our conclusion from these data relating the size of breast carcinoma to operability is that large size alone, unaccompanied by other clinical signs of local advancement of the disease, is certainly not a contraindication to radical mastectomy When large size is associated with any one of the five local signs of grave significance the hope for cure by operation is so small that the choice between surgery and irradiation is very difficult, and I have no strong preference for one or the other

Multiple Carcinomas in One Breast Related to Operability Multiple carcinomas in one breast that are evident clinically are comparatively infrequent. In our Presbyterian Hospital data there are a total of only 31 such cases As indicated in Table 109 the results of radical mastectomy in the 27 patients in whom multiplicity of the carcinoma was the only sign of advanced local disease were as good as the results in our series of radical mastectomies as a whole

Our conclusions regarding the significance of multiplicity of carcinoma in one breast are similar to those regarding large size Multiplicity alone is not a contraindication to operation. Our cases in which multiplicity was associated with any one of the local signs of grave significance are too few to justify any definite conclusions but the data certainly do not encourage surgery

Redness of the Skin Related to Operability. I have mentioned redness of the skin over breast carcinoma—when not of the inflammatory type—as being due to involvement of the skin by the disease or to necrosis in the tumor.

In Table 110 the results of operation in a total of 75 cases with redness of the skin are shown. Our cases of inflammatory carcinoma have been excluded, of

Table 110. Results of Radical Mastectomy in Carcinoma with Redness of the Skin—Categorically Inoperable Cases Excluded

(Presbyterian Hospital, 1915–1942)

Group of cases	No. of cases	Local recurrence		5-yr. clinical cure	
		No.	Per cent	No.	Per cent
I Total patients Radical mastectomy	1058	169	16.0	477	45.1
II Redness of the skin *only*	33	7	21.2	14	42.4
III Redness of the skin *with* any one of 5 grave signs of locally advanced disease	42	17	40.5	8	19.0

course, from this table together with other categorically inoperable cases. In our patients with redness of the skin unaccompanied by other clinical features of locally advanced disease, operation gave approximately as good results as it did in our series of cases of carcinoma as a whole. The local recurrence rate doubled and the cure rate was only half as good when redness was accompanied by any one of the five grave signs of locally advanced disease.

It seems fair to conclude from our experience that *redness of the skin* over a carcinoma is, in itself, not a contraindication to operation. When it is accompanied by any one of the five grave signs of locally advanced disease, however, the results of surgery are so poor that there is little to choose between surgery and irradiation.

Skin Involvement Related to Operability. Involvement of the skin over carcinoma, as we have used it in our classification, refers to those cases in which the skin over the tumor has become fixed and immovable. It is tied down by fibrosis developing over the carcinoma or by actual infiltration of the derma by carcinoma cells. This is a clinical and not a pathological criterion. Cases in which skin involvement has progressed to the point of ulceration are not included; they form a group which I shall discuss separately.

Our results in a total of 116 cases with involvement of the skin are shown in Table 111. When such involvement was the only sign of locally advanced disease the results of operation were approximately the same as in our series of radical mastectomies as a whole. But when involvement of the skin was accompanied by any one of the five grave signs of locally advanced disease the cure rate was reduced by more than half.

Our data therefore indicate that involvement of the overlying skin by the carcinoma is in itself no contraindication to surgical treatment. When, in addition,

Table 111 Results of Radical Mastectomy in Cases with Skin Involvement—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I. Total patients Radical mastectomy	1058	169	16	477	45 1
II. Involvement of skin *only*	58	10	17 2	25	44 8
III. Involvement of skin *with* any one of the 5 grave signs of locally advanced disease	58	13	22 4	10	17 2

any one of the five grave signs of locally advanced disease is present, surgery is comparatively unsuccessful, and I do not have any strong preference for it over irradiation

Ulceration of the Skin Related to Operability Ulceration of the skin over a carcinoma is merely a more advanced stage of the process of involvement of the skin by the disease which I have been discussing But ulceration becomes a grave sign of locally advanced disease because when this stage is reached there are not many cases left in which the disease has not become obviously inoperable for other reasons. Our data shown in Table 112, therefore include only 27 cases with ulceration of the skin in which radical mastectomy was done

Table 112. Results of Radical Mastectomy in Cases with Ulceration of Skin—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No. of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I. Total patients Radical mastectomy	1058	169	16	477	45 1
II. Ulceration of skin *only*	14	2	14 3	5	35 7
III Ulceration of skin *with* any other grave sign of locally advanced disease	13	4	30 8	0	

The results of radical mastectomy in our patients who have had ulceration of the skin, without any other sign of locally advanced disease, have not been as good as in our series of radical mastectomies as a whole, but they have been good enough to encourage us to continue to operate on these patients. When ulceration of the skin has been associated with any of the other grave signs of locally advanced disease, however our results with operation have been so bad that I

am opposed to radical mastectomy for these patients Irradiation is a better form of treatment for them

Edema of the Skin Related to Operability I have already described, in Chapter 18, the blockage of the subdermal lymphatics by emboli of carcinoma cells which is the underlying cause of edema of the skin The grave prognostic significance of this clinical sign is therefore at once apparent In order to assess as accurately as possible the significance of edema Dr Stout and I classified the cases with edema into two groups

(1) Those in which the extent of the edema was limited to less than one-third of the skin over the breast

(2) Those in which the edema involved a larger area of skin

I have already pointed out that none of our patients with the latter more extensive form of edema were cured by operation

Table 113. Results of Radical Mastectomy in Cases with Limited Edema of the Skin—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I Total patients Radical mastectomy	1058	169	16	477	45 1
II Limited edema *only*	75	24	32	17	22 7
III Limited edema *with* any other grave sign of locally advanced disease	24	14	58 3	0	

I am here concerned with the prognostic significance of edema of only limited extent Table 113 shows our data regarding 99 cases in which this sign was present In 75 patients in whom limited edema was the only evident sign of advanced disease radical mastectomy achieved only approximately half the cure rate that it achieved in our series of breast carcinomas as a whole And in 24 patients in whom limited edema was associated with one or more of the other grave signs of locally advanced disease operation did not cure a single one

This experience indicates that even a limited amount of edema is an extremely grave prognostic sign It is perhaps permissible to perform radical mastectomy when limited edema is the only indication of advanced disease, but the association of edema of even limited extent with any of the other grave signs of locally advanced carcinoma is an absolute contraindication to operation

Fixation of the Carcinoma Related to Operability In Chapter 5 I described the phenomenon of fixation of breast carcinoma to the underlying pectoral fascia and muscle and finally to the thoracic cage, and my classification of fixation in three degrees First and second degree fixation are early evidences of fixation, demonstrated by pectoral contraction in the sitting and in the supine positions

Third degree fixation is the advanced stage in which the carcinoma is immovably fixed to the chest wall

The surgeons who described the physical findings in the breast carcinomas in our Presbyterian Hospital data in years gone by did not in general distinguish the lesser degrees of fixation which I have described They recorded only solid fixation to the chest wall I am therefore able to present data from our Presbyterian Hospital 1915–1942 series only in regard to third degree fixation These data are shown in Table 114 There were a total of 47 patients with third degree fixation of their carcinomas Whether or not the third degree fixation was associated with another grave sign of locally advanced disease made little difference operation failed to cure in almost all I am therefore opposed in general to radical mastectomy for carcinoma that is solidly fixed to the chest wall

Table 114. Results of Radical Mastectomy in Cases in Which There Was Third Degree Fixation of the Tumor to the Chest Wall—Categorically Inoperable Cases Excluded
(Presbyterian Hospital 1915–1942)

Group of cases	No. of cases	Local recurrence		5-yr clinical cure	
		No.	Per cent	No	Per cent
I. Total patients Radical mastectomy	1058	169	16	477	45 1
II. 3rd degree fixation, *only*	20	8	40	1	5
III. 3rd degree fixation *with* any other grave sign of locally advanced disease	27	10	37	1	3 7

There is one exception in regard to the grave prognostic significance of solid fixation. It is that carcinomas occurring in the inframammary fold are occasionally solidly fixed but are still not advanced and are perfectly curable by surgery This paradox is explained by the anatomy of the inframammary fold. The superficial fascia enclosing the breast fuses with the deep fascia of the abdominal wall along the lower edge of the breast A carcinoma developing in the lower edge of the breast may therefore be solidly fixed at an early stage of its evolution because the fibrosis around it ties it down to the deep fascia If there are no other contraindications, such fixed inframammary carcinomas should be operated upon Great care should be taken in the regional dissection of course, to remove the fascia over the upper external oblique muscle as well as the upper rectus fascia, in continuity with the pectoralis major and the overlying breast. The following case is an example of successful surgical attack upon one of these solidly fixed inframammary carcinomas

Mrs. D B., a woman lawyer aged 50 had noticed a lump at the inner end of the lower margin of the right breast, five months before she consulted me. It had enlarged slowly

Inspection of the breasts in the sitting position showed them to be symmetrical. When the patient lay supine, however there was an obvious tumor at the inner end

am opposed to radical mastectomy for these patients Irradiation is a better form of treatment for them

Edema of the Skin Related to Operability I have already described, in Chapter 18, the blockage of the subdermal lymphatics by emboli of carcinoma cells which is the underlying cause of edema of the skin The grave prognostic significance of this clinical sign is therefore at once apparent In order to assess as accurately as possible the significance of edema Dr Stout and I classified the cases with edema into two groups

(1) Those in which the extent of the edema was limited to less than one-third of the skin over the breast

(2) Those in which the edema involved a larger area of skin

I have already pointed out that none of our patients with the latter more extensive form of edema were cured by operation

Table 113. Results of Radical Mastectomy in Cases with Limited Edema of the Skin—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I Total patients Radical mastectomy	1058	169	16	477	45 1
II Limited edema *only*	75	24	32	17	22 7
III Limited edema *with* any other grave sign of locally advanced disease	24	14	58 3	0	

I am here concerned with the prognostic significance of edema of only limited extent Table 113 shows our data regarding 99 cases in which this sign was present In 75 patients in whom limited edema was the only evident sign of advanced disease radical mastectomy achieved only approximately half the cure rate that it achieved in our series of breast carcinomas as a whole And in 24 patients in whom limited edema was associated with one or more of the other grave signs of locally advanced disease operation did not cure a single one

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Fixation of the Carcinoma Related to Operability In Chapter 5 I described the phenomenon of fixation of breast carcinoma to the underlying pectoral fascia and muscle and finally to the thoracic cage, and my classification of fixation in three degrees First and second degree fixation are early evidences of fixation, demonstrated by pectoral contraction in the sitting and in the supine positions

Third degree fixation is the advanced stage in which *the carcinoma is immovably fixed to the chest wall*

The surgeons who described the physical findings in the breast carcinomas in our Presbyterian Hospital data in years gone by did not in general distinguish the lesser degrees of fixation which I have described They recorded only solid fixation to the chest wall I am therefore able to present data from our Presbyterian Hospital 1915–1942 series only in regard to third degree fixation These data are shown in Table 114 *There were a total of 47 patients with third degree fixation of their carcinomas.* Whether or not the third degree fixation was associated with another grave sign of locally advanced disease made little difference operation failed to cure in almost all I am therefore opposed in general to radical mastectomy for carcinoma that is solidly fixed to the chest wall

Table 114. Results of Radical Mastectomy in Cases in Which There Was Third Degree Fixation of the Tumor to the Chest Wall—Categorically Inoperable Cases Excluded
(Presbyterian Hospital 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I. Total patients Radical mastectomy	1058	169	16	477	45 1
II. 3rd degree fixation, *only*	20	8	40	1	5
III. 3rd degree fixation *with* any other grave sign of locally advanced disease	27	10	37	1	3 7

There is one exception in regard to the grave prognostic significance of solid fixation It is that carcinomas occurring in the inframammary fold are occasionally solidly fixed but are still not advanced and are perfectly curable by surgery This paradox is explained by the anatomy of the inframammary fold The superficial fascia enclosing the breast fuses with the deep fascia of the abdominal wall along the lower edge of the breast. A carcinoma developing in the lower edge of the breast may therefore be solidly fixed at an early stage of its evolution because the fibrosis around it ties it down to the deep fascia. If there are no other contraindications, such fixed inframammary carcinomas should be operated upon Great care should be taken in the regional dissection, of course, to remove the fascia over the upper external oblique muscle as well as the upper rectus fascia, in continuity with the pectoralis major and the overlying breast. The following case is an example of successful surgical attack upon one of these solidly fixed inframammary carcinomas

Mrs. D B a woman lawyer aged 50 had noticed a lump at the inner end of the lower margin of the right breast, five months before she consulted me. It had enlarged slowly

Inspection of the breasts in the sitting position showed them to be symmetrical When the patient lay supine, however there was an obvious tumor at the inner end

of the inframammary fold of the right breast, as shown in my sketch (Fig 336) The tumor was 3 cm in diameter, hard, fairly well delimited, and firmly fixed to the underlying chest wall There was definite dimpling of the skin over it but no redness or edema

In the lower right axilla there was a chain of three 1 cm firm nodes which I thought represented metastases

There was in addition in the same breast a rounded, movable, 1 cm nodule beneath the areolar edge on the radius of 5 o'clock I thought this represented a cyst

Films of the skeleton and chest showed no evidence of metastasis

At operation the inframammary tumor was biopsied and proved to be a carcinoma of the circumscribed type Radical mastectomy was carried out The subareolar tumor was a simple cyst Twenty-two lymph nodes were recovered from the axilla and none contained metastasis The patient was well ten years later

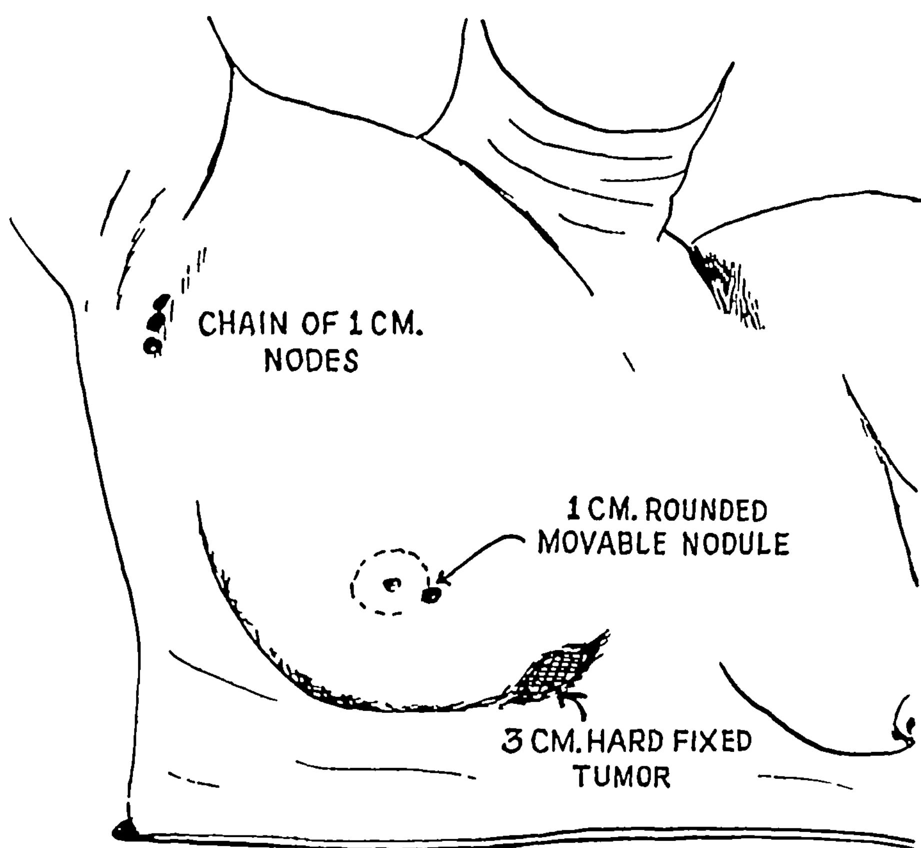


Fig 336 Carcinoma at inner end of inframammary fold with third degree firm fixation to deeper structures

For an estimate of the significance of first and second degree fixation of the carcinoma I have to turn to the records of my own series of 356 personal cases In these patients I myself described the carcinoma and noted the presence or absence of first and second degree fixation Table 115 shows these data

It is apparent from this series of cases that neither first nor second degree fixation had any demonstrable untoward prognostic significance The results of radical mastectomy were apparently the same in patients in whom such fixation was the only sign of advanced disease as they were in my series of personal cases as a whole First and second degree fixation are not, therefore, in themselves, any contraindication to radical mastectomy When these types of fixation were associated with any other sign of locally advanced disease the local recurrence

rate rose and the cure rate fell markedly In cases of this type the choice of surgery versus irradiation is difficult and had best be decided by the regional lymph node biopsy techniques which I must now describe

3 *Regional Lymph Node Metastases Related to Operability* Fifteen years ago when Dr Stout and I began analyzing our Presbyterian Hospital data in search of criteria of operability the only indications we had of the presence and extent of regional metastases in axillary internal mammary and supraclavicular lymph nodes were based upon palpation of these lymph node regions During the

Table 115. Results of Radical Mastectomy in Cases in Which There Was First and Second Degree Fixation of the Tumor to the Chest Wall

Personal Series—Cases of Third Degree Fixation Excluded

(Presbyterian Hospital 1935–1950)

Group of cases	No of cases	5-year local recurrence		5-yr clinical cure	
		No.	Per cent	No.	Per cent
I. Entire series	356	54	15 2	202	56 7
II. 1st degree fixation *only*	81	12	14 8	44	54 3
III. 1st degree fixation *with* any one of 5 grave signs of locally advanced disease	16	5	31 2	2	12.5
IV 2nd degree fixation *only*	33	7	21 2	19	57 6
V 2nd degree fixation *with* any one of 5 grave signs of locally advanced disease	10	5	50 0	3	33 3

last five years these clinical criteria have, to a great extent, been superseded by the pathological evidence that we obtain by biopsy of these regional lymph nodes It seems worth while nevertheless, to present here what we learned concerning the significance of the findings of palpation first because these findings still have a good deal of significance and secondly because most surgeons are not yet performing regional node biopsies, having yet to be convinced of their value.

Massively Enlarged Axillary Lymph Nodes Related to Operability Although axillary palpation is an inaccurate guide to the presence of metastases in axillary lymph nodes when the lymph nodes are small, palpation is highly accurate when the nodes are large. I have documented, in Chapter 5 our microscopical findings in cases in which the transverse diameter of the nodes measured clinically was 2.5 cm or more metastases were found in 98 per cent. For purposes of classification we have called nodes measuring 2 5 cm or more clinically *massively enlarged.*

Our data regarding the prognostic significance of massively enlarged nodes are shown in Table 116 We had a total of 43 such cases in which radical mas-

Table 116 Results of Radical Mastectomy in Cases with Massive Enlargement of Metastatic Axillary Lymph Nodes—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I Total patients Radical mastectomy	1058	169	16	477	45 1
II 2 5 cm nodes *only*	24	3	12 5	9	37 5
III 2 5 cm nodes *with* any other grave sign of locally advanced disease	19	9	42 1	1	5 3

tectomy was done In the 24 in which the massive enlargement of the nodes was the only sign of advanced disease, the cure rate was slightly reduced, but not enough to justify enlarged nodes of this size being regarded as a contraindication to operation The results in 19 cases in which the feature of massively enlarged nodes was associated with one or more of the other grave signs of locally advanced disease, however, were very poor Almost half of the patients had local recurrence and only one remained free of evidence of disease at the end of five years This experience convinces me that these patients should be treated with irradiation and not by surgery

Fixation of Axillary Lymph Nodes As metastases grow in axillary lymph nodes the disease breaks through the capsule of the nodes and invades the axillary fat and connective tissue The nodes finally become fused together and fixed to the chest wall deeply and to the skin of the axilla superficially Fixation to the axillary skin may be apparent as a zone of skin dimpling

Our data regarding the results of radical mastectomy in patients with fixed axillary lymph nodes containing metastases are shown in Table 117 The results

Table 117 Results of Radical Mastectomy in Cases with Fixed Metastatic Axillary Nodes—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I Total patients Radical mastectomy	1058	169	16	477	45 1
II Fixed axillary nodes *only*	8	1	12 5	1	12 5
III Fixed axillary nodes *with* any other grave sign of locally advanced disease	18	9	50	0	

of operation were so poor in all cases in which the axillary nodes were fixed whether this feature was present alone or in association with one of the other grave signs of locally advanced disease, that I believe that in general these patients should be treated with irradiation and not by surgery Today I would biopsy the apex of the axilla and the internal mammary areas in patients with massively enlarged or fixed axillary lymph nodes, and obtain more reliable information as to the extent of the disease before deciding what treatment to give

From the correlations of the clinical features of our Presbyterian Hospital breast carcinoma with the results of operation which I have presented in Tables 101 to 117 Dr Stout and I drew a list of *clinical criteria of operability* which we tested and refined over a period of years and presented in their final form in 1951 The only important change that we made in the final version of the criteria as compared with the original version was the omission of the interdiction of operation for carcinoma developing during pregnancy and lactation

Clinical Criteria of Operability The *clinical criteria of operability* in their final form were as follows Carcinoma of the breast in women of all age groups who are in good enough general condition to withstand operation should be treated by radical mastectomy except when

1 Extensive edema of the skin over the breast is present.
2. Satellite nodules are present in the skin over the breast.
3 The carcinoma is of the inflammatory type.
4 Parasternal tumor nodules are present
5 Proved supraclavicular metastases are present.
6 There is edema of the arm.
7 Distant metastases are demonstrated
8 Any two, or more, of the following grave signs of locally advanced carcinoma are present
   a. Ulceration of the skin.
   b Edema of the skin of limited extent (less than one-third of the skin over the breast involved)
   c. Solid fixation of the tumor to the chest wall.
   d. Axillary lymph nodes measuring 2.5 cm., or more, in transverse diameter
   e. Fixation of the axillary lymph nodes to the skin or the deep structures of the axilla.

It was fortunate indeed for the purposes of the inquiry as to operability that Dr Stout and I were carrying out that several of our attending surgeons at the Presbyterian Hospital spurred on by the most idealistic of motives, had performed radical mastectomy on types of cases which were clearly inoperable according to our criteria. In this manner our criteria have been well tested in our own hospital where our records are sufficiently complete to provide an adequate test. The application of our clinical criteria of operability to our Presbyterian Hospital 1915–1942 series of carcinomas treated by radical mastectomy is shown in Table 118

Study of this table shows that a total of 120 cases fall into the inoperable group of which 77 were inoperable because they were in our so-called categorically inoperable class, while 43 were inoperable because two or more of the five grave signs of locally advanced carcinoma were present Half of these 120 patients with inoperable disease who were nevertheless operated upon are known to have developed local recurrence and only one was free of evidence of disease

Table 116. Results of Radical Mastectomy in Cases with Massive Enlargement of Metastatic Axillary Lymph Nodes—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I Total patients Radical mastectomy	1058	169	16	477	45 1
II 2 5 cm nodes *only*	24	3	12 5	9	37 5
III 2 5 cm nodes *with* any other grave sign of locally advanced disease	19	9	42 1	1	5 3

tectomy was done In the 24 in which the massive enlargement of the nodes was the only sign of advanced disease, the cure rate was slightly reduced, but not enough to justify enlarged nodes of this size being regarded as a contraindication to operation The results in 19 cases in which the feature of massively enlarged nodes was associated with one or more of the other grave signs of locally advanced disease, however, were very poor Almost half of the patients had local recurrence and only one remained free of evidence of disease at the end of five years This experience convinces me that these patients should be treated with irradiation and not by surgery

Fixation of Axillary Lymph Nodes As metastases grow in axillary lymph nodes the disease breaks through the capsule of the nodes and invades the axillary fat and connective tissue The nodes finally become fused together and fixed to the chest wall deeply and to the skin of the axilla superficially Fixation to the axillary skin may be apparent as a zone of skin dimpling

Our data regarding the results of radical mastectomy in patients with fixed axillary lymph nodes containing metastases are shown in Table 117 The results

Table 117 Results of Radical Mastectomy in Cases with Fixed Metastatic Axillary Nodes—Categorically Inoperable Cases Excluded
(Presbyterian Hospital, 1915–1942)

Group of cases	No of cases	Local recurrence		5-yr clinical cure	
		No	Per cent	No	Per cent
I Total patients Radical mastectomy	1058	169	16	477	45 1
II Fixed axillary nodes *only*	8	1	12 5	1	12 5
III Fixed axillary nodes *with* any other grave sign of locally advanced disease	18	9	50	0	

Table 119 Mean Total Duration of Breast Carcinoma—Onset to Death—in Various Groups of Cases

I.	777 untreated cases collected by Wade from various published sources	38 55 months
II	77 Presbyterian Hospital cases (1935–1942) classified as inoperable and treated by radiotherapy only	40 4 months
III	38 Presbyterian Hospital cases (1915–1942) classified as inoperable but treated by simple mastectomy	37 4 months
IV	120 Presbyterian Hospital cases (1915–1942) classified as inoperable but treated by radical mastectomy	33 0 months

were treated by simple mastectomy or by irradiation Those treated by irradiation lived slightly longer than the untreated patients in Wade s collected series. There are, of course several possible interpretations of these facts, but they at least suggest that the more surgery performed upon patients with inoperable carcinoma the shorter will be their survival This is in agreement with our understanding of the mechanism of metastasis A surgeon dissecting in tissues infiltrated by carcinoma can be expected to produce showers of carcinoma emboli which should hasten death I believe that I have observed this clinical phenomenon a number of times.

Our clinical criteria of operability have been tested and found useful not only in our own clinic but in various hospitals in this country and abroad (Tomlinson and Eckert, Wells, Dahl Iversen and Soerensen)

Biopsy Determination of Extent of Breast Carcinoma

I am well aware, however that we are yet far from achieving the ideal that should be our goal in the selection of patients for operation namely *criteria which will make it possible to exclude all of the patients who have no chance of cure* Our clinical criteria enabled us to sort out a proportion of the cases in which the disease had spread beyond the scope of radical mastectomy but there were two important weaknesses in this method of selection One was the lack of a dependable method for determining the existence of occult regional lymph node metastases at the periphery of the operative field—in the internal mammary nodes, the nodes at the apex of the axilla, and the supraclavicular nodes The other weakness was our inability to detect distant metastases in bone By employing biopsy we have attempted to remedy both of these defects in our method of selection of patients for operation In substituting criteria based on pathological evidence of the spread of the disease, for our clinical criteria based on palpation, we have made an important improvement in our ability to select the patients who can be cured by operation

In my account in Chapter 19 of the routes of metastases of mammary carcinoma I described regional lymph node metastases occurring first in the mid axillary nodes. After the axillary lymph node filter has been partially blocked, metastases are found in the internal mammary lymph nodes in the upper three interspaces in from 30 to 50 per cent of the cases The third stage in the process of lymphatic extension is involvement of the nodes at the apex of the axilla. In the final stage of regional lymph node metastasis the supraclavicular nodes are affected. Carcinoma emboli reach the deep inferior cervical sentinel nodes at the

after five years. This one patient was not a permanent cure. Operation was worth while in her case only because she had a particularly favorable type of carcinoma —the circumscribed type.

Her story was as follows:

Mrs. L. P., a Negro housewife aged 43, was admitted to Presbyterian Hospital for a tumor of the right breast which she said she had had for one year. Examination showed the right breast filled with a huge, firm, rounded tumor measuring 12 x 15 cm. in diameter. It was centered in the upper outer sector of the breast where it appeared to have arisen. The skin over the tumor was reddened and adherent. The nipple was retracted. The tumor was solidly fixed to the underlying chest wall. There was a chain of massively enlarged firm nodes running from the tumor up into the axilla.

Table 118. Clinical Criteria of Operability Applied to Presbyterian Hospital Series of Radical Mastectomies 1915–1942

Group of cases	No. of cases	5-yr. local recurrence		5-yr. clinical cures	
		No.	Per cent	No.	Per cent
I. Cases in which radical mastectomy was performed (1915–1942)	1135	225	19.8	477	42.0
II. Cases that would be classed as *inoperable*					
1. Categorically inoperable group	77	41	53.2	0	
2. Combination of 5 grave signs of locally advanced disease	43	18	42.0	1	2.3
III. Cases that would be classed as *operable*	1015	166	16.4	476	46.9

Despite the advanced local extent of the carcinoma, radical mastectomy was done. The carcinoma proved to be of the circumscribed type. There were several lymph nodes that grossly measured 2.5 cm. in diameter. All were replaced by carcinoma.

The patient's first recurrence was noted in the operative field on the chest wall five and a half years after operation. Metastases subsequently appeared in both supraclavicular areas, the contralateral axilla, and in the chest. She died eight years after operation.

If the clinical criteria of operability which I have described had been followed in the selection of our Presbyterian Hospital cases for radical mastectomy, 120, or some 10 per cent, of the operations would have been avoided, without foregoing permanent cure in a single patient.

It may be asked what effect radical mastectomy had on the length of life in these patients whose carcinomas were inoperable. Table 119 attempts to answer the question from our data. It will be seen that the average mean duration of life from onset of symptoms to death was shorter in the patients with inoperable carcinoma who were treated by radical mastectomy than it was in those who

The intercostal muscle having been gotten out of the way a very delicate layer of fascia spanning the intercostal space and covering the areolar tissue in which the internal mammary vessels and lymphatic trunks and small lymph nodes lie is exposed This film of fascia is incised and the delicate process of removing the areolar tissue, and what lymph nodes can be found is begun (338 *D*) This is

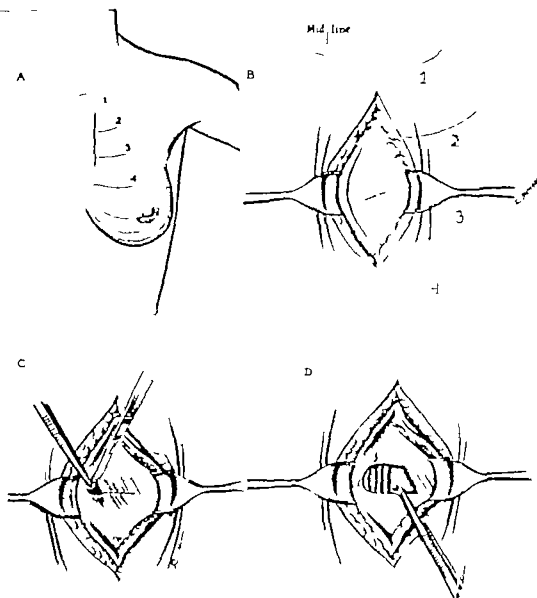


Fig. 338 Technique of internal mammary biopsy *A* the skin incision *B* detaching the pectoralis major muscle to reveal the interspace. *C* excising the intercostal muscle to expose the contents of the interspace. *D* dissection of the areolar tissue and lymph nodes from the interspace

achieved best in my hands, with what I call the micro-peanut This is made by rolling a bit of five meshed gauze into a ball about 1 mm in diameter and clamping it in the tip of a fine-curved Halsted hemostat Figure 339 shows one of these instruments The areolar tissue surrounding the internal mammary vein or veins and artery is cleared from these vessels with these micro-peanuts and removed with fine thumb-forceps As the interspace is cleared one or sometimes two small nodes will usually be encountered They are often not more than 2 to 4 mm

confluence of the internal jugular and subclavian veins either through the subclavian lymphatic trunks from the axilla or through the internal mammary lymphatic trunk The progression of the disease in these regional lymph node groups is shown diagrammatically in Figure 337 We have used biopsy as a method of documenting the stage of the disease in these terms in the individual patient

Internal Mammary Biopsy. Richard Handley began, in 1947, to remove the internal mammary node in the second interspace at the completion of radical mastectomy It was his report of his findings that gave me the idea of biopsying the internal mammary area *before operation* in an effort to determine operability

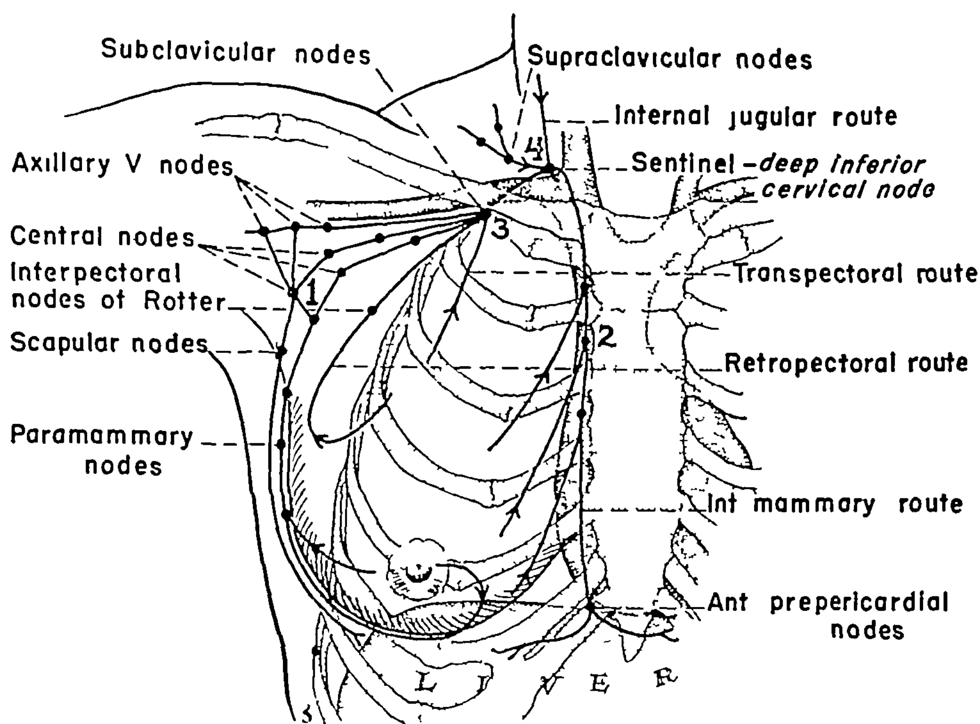


Fig 337 The sequence of metastasis in the regional lymph node filter in carcinoma of the breast

more accurately In 1952 I began by exploring the second interspace, as Handley had done, but I soon realized that all of the upper three interspaces should be explored if an accurate estimate of the presence of internal mammary metastases is to be had

Our technique for the procedure is as follows The skin incision (Fig 338 *A*) is made along the edge of the sternum from the lower edge of the first rib to the upper edge of the fourth rib We investigate one interspace at a time, beginning usually with the 2nd interspace because it is easier to explore than the 1st interspace The attachment of the pectoralis major to the sternum is severed (Fig 338 *B*) to afford adequate access to the interspace being investigated The intercostal (internal) muscle is then excised (Fig 338 *C*) from the inner end of the interspace for a distance of about 2 cm lateral to the sternal edge Great care is necessary in this step to identify and secure the perforating vessels and their branches If hemostasis is not complete bleeding will obscure the small operative field and make dissection of the internal mammary vessels impossible

The intercostal muscle having been gotten out of the way a very delicate layer of fascia spanning the intercostal space and covering the areolar tissue in which the internal mammary vessels and lymphatic trunks and small lymph nodes lie is exposed. This film of fascia is incised and the delicate process of removing the areolar tissue, and what lymph nodes can be found is begun (338 *D*) This is

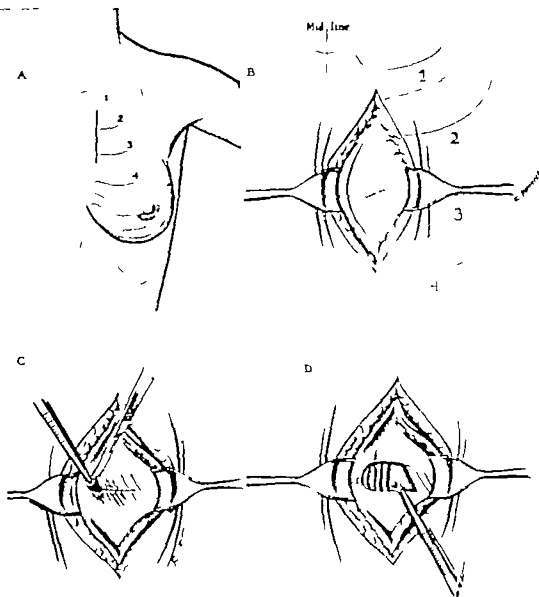


Fig. 338 Technique of internal mammary biopsy *A* the skin incision. *B* detaching the pectoralis major muscle to reveal the interspace. *C* excising the intercostal muscle to expose the contents of the interspace. *D* dissection of the areolar tissue and lymph nodes from the interspace.

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in diameter They may be partially hidden beneath the edges of the costal cartilages or the sternum, from which they have to be fished out with a fine curved Halsted hemostat This is an essential instrument in performing this dissection

When the dissection is completed the internal mammary vessels lie bare upon the pleura, beneath which the lung can be seen moving In a few cases we have put a small hole through the pleura during the dissection but no harm has come from it When this has occurred we take care to have a postoperative x-ray film of the chest to make sure no appreciable amount of air remains in the pleural cavity If necessary, we aspirate it One precaution which will minimize the chance of entering the pleura is not to carry the dissection of the interspace more than 3 cm laterally from the sternal edge

We close the subcutaneous fat and the skin in layers over the dissected interspaces, without drainage

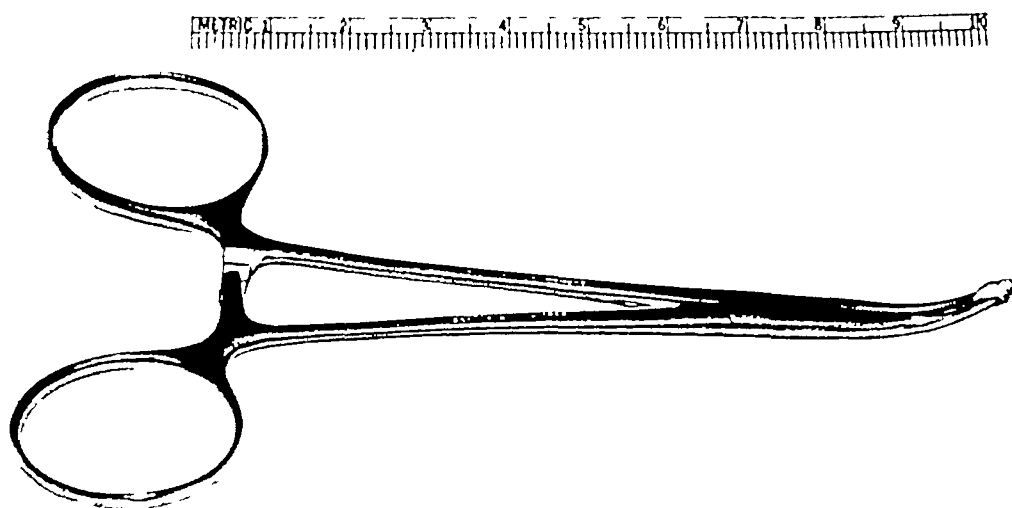


Fig 339 The micro-peanut used for dissection of the interspace

Every minute bit of areolar tissue removed from each interspace, as well as the lymph nodes, is put at once into a small bottle of Bouin's fixative kept at the operating table These small pieces of tissue dry out very quickly if left lying about on gauze, and the cellular detail is ruined We embed these tissues in paraffin and cut them in a number of levels

We utilize frozen sections only if we find grossly evident disease in an interspace If we find this condition in the first interspace explored, we terminate our biopsy Otherwise we usually explore all three upper interspaces We leave the first interspace to the last because it is the most difficult This difficulty is due partly to the fact that it is usually narrower than the others, and partly because this interspace is inclined toward the base of the neck instead of being in the horizontal plane of the chest wall as are the other interspaces This inclination makes access to it difficult To our knowledge we have done our patients no harm with these internal mammary biopsies It is true that the vertical parasternal scar is not desirable, but it is a small price for making certain that a futile radical mastectomy is not done

The results of our internal mammary biopsies are summarized in Table 120

Metastases were found in 31 6 per cent of the cases. This frequency must be interpreted in terms of the types of cases biopsied It was not possible in either the Francis Delafield Hospital or the Presbyterian Hospital to perform these biopsies on all the patients. In the former hospital where the patients are all ward patients from the lowest income brackets breast carcinoma is seen, in general at a more advanced stage than in the Presbyterian Hospital, where both ward and private patients are treated At the Francis Delafield Hospital we have performed internal mammary biopsy on all patients with primary breast carcinoma in whom the disease is early enough for any consideration of surgical treatment The fact that we performed internal mammary biopsy in only 153 of the total of 271 primary cases of breast carcinoma admitted to the Francis Delafield Hospital during the period 1952–1955 is an indication of the comparatively

Table 120. Internal Mammary Biopsies—Carcinoma of Breast
(Presbyterian Hospital and Francis Delafield Hospital, 1952–1955)

Hospital	No of cases primary breast ca.	No of cases int. mam. biopsy	Negative		Positive	
			No	Per cent	No	Per cent
Francis Delafield	271	153	96	62 7	57	37 3
Presbyterian	450	151	112	74 2	39	25 8
Total	721	304	208	68 4	96	31 6

advanced stage of the disease in these patients In the Presbyterian Hospital internal mammary biopsy has been used to only a limited extent by a few of the attending surgeons We have found it necessary in general to perform these biopsies at a separate preliminary operative session so that we can study the biopsy specimens in paraffin sections cut at a number of levels This adds an additional operative session, and the time and expense that goes into it, if radical mastectomy is finally decided upon From the practical point of view this forces us to limit these biopsies to patients in whom there is a considerable likelihood of finding internal mammary metastases

We do not yet know enough however to define precisely which patients these are. The evidence that I have presented in Chapter 19 suggests that the three most significant factors favoring internal mammary metastases are in order of their importance

1 Axillary metastases.
2. Large size of the primary tumor The critical size is somewhere between 3 and 5 cm.
3 Situation of the primary tumor in the central or medial half of the breast (zones, C, D E, F and G)

The clinical follow up data from my personal series of cases treated by radical mastectomy although not large enough to be decisive, suggest that only the carcinomas situated in the lower parasternal zone (zone D) are more likely to metastasize to the internal mammary nodes Table 121 shows the frequency of

parasternal recurrence after radical mastectomy, which is of course the clinical indication of internal mammary metastases, in my personal series of 356 cases It will be noted that there were about the same number of parasternal recurrences from tumors of the outer half of the breast (zones A and B) as from tumors of the center and inner half of the breast (zones C, F, and G), excepting the parasternal zones (D and E)

An example of metastasis to the internal mammary nodes from a carcinoma of the outer half of the breast is shown in my sketch (Fig 340) of Mrs A K She

Table 121 Parasternal Metastases and Local Recurrences by Site of Tumor Following Radical Mastectomy

(Personal Series, 1935–1950)

	Axillary Nodes not Involved				Axillary Nodes Involved			
Zone in breast	No of cases	Parasternal nodule	Local recurr	Total no rec	No of cases	Parasternal nodule	Local recurr.	Total no rec
A	52	2	—	2	105	4	13	17
B	19	—	—	—	15	1	5	6
C	6	—	—	—	8	1	2	3
D	6	2	—	2	3	1	1	2
E	7	1	—	1	3	—	1	1
F	24	1	—	1	16	1	1	2
G	44	1	—	1	46	2	14	16
Diffuse	1	—	—	—	—	—	—	—
Indeterm	1	—	—	—	—	—	—	—
Total	160	7	—	7	196	10	37	47

was a woman of 70 with a 5 cm carcinoma situated in zone B It had produced skin retraction and 1st degree fixation The nipple was deviated downward toward the tumor There was a 3 cm firm, movable node in the axilla Internal mammary biopsy showed metastasis in a 3 mm node from the 2nd interspace

I would guess that our finding of internal mammary metastases in 31 6 per cent of the patients in whom we have done these biopsies is an approximation of the true frequency of such metastases in the average unselected case series Our figure is very close to Handley's finding of 33 per cent of internal mammary metastases in his series of 150 Middlesex Hospital cases It is distinctly higher than Dahl-Iversen's figure of 19 7 per cent of internal mammary metastases in his consecutive series of 229 cases done at the Rigshospitalet But Dahl-Iversen's case material has been exceptionally favorable to judge from the low incidence of axillary metastases in his cases It has been only 45 9 per cent as compared with our incidence of 61 6 per cent

Since our patients in whom internal mammary metastases were found to be present did not, except in a few special instances, have radical mastectomy, we do not know the relationship of internal mammary metastases to axillary metastases in our series of cases As I have documented in Chapter 19, data from other clinics indicate that internal mammary metastases are found in only about 5 per cent of the patients who do not have axillary metastases

Supraclavicular Biopsy Dahl-Iversen of Copenhagen began in 1947 (1st

series of cases) to dissect out the supraclavicular nodes as part of his surgical attack upon mammary carcinoma He has since continued this practice in his 3rd and 4th series of cases performing the extended operation upon a total of 274 patients He has found supraclavicular metastases in 8 4 per cent In all these cases the supraclavicular metastases were occult, none being palpable No supra clavicular metastases were found in patients who did not have axillary metas tases

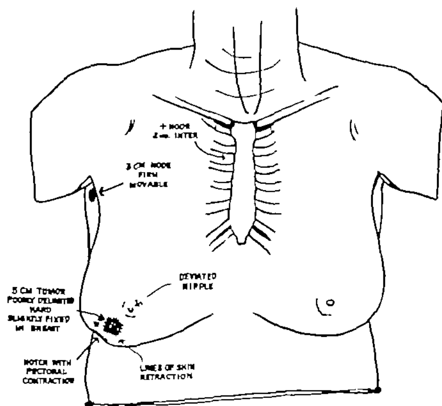


Fig. 340 A 5 cm carcinoma of the lower outer zone of the breast with metastasis to the internal mammary node in the second interspace.

It was Dahl Iversen s startling 1949 report of his finding supraclavicular metastasis in 33 per cent of his first series of cases that stimulated us to include supraclavicular dissection as part of our preliminary biopsy procedure for assessing operability Our hope was that this procedure would reveal occult supra clavicular metastasis in a certain number of patients whose breast carcinomas were otherwise operable and that in this manner we would avoid performing futile radical mastectomy There is very little doubt in my mind but that patients with supraclavicular metastasis are incurable by surgery As I have already pointed out in Chapter 19 the disease has almost always escaped into the blood stream when it reaches the signal node of the supraclavicular group lying upon the confluence of the internal jugular and subclavian veins

Halsted s experience long ago confirmed this fact Among 119 of his patients in whom supraclavicular dissection was done, 44 were found to have metastases in these nodes Only two were cured for five years or more Dahl Iversen has three five year cures among 17 cases with microscopic metastases in the supraclavicular nodes. My impression is nevertheless that radiotherapy is preferable to surgery when the disease has reached this stage

Our *technique* for our supraclavicular biopsy has been the standard one for supraclavicular dissection The skin incision is an oblique one across the base of the neck The external jugular vein is sacrificed The sternocleidomastoid is retracted medially, and the triangle which is bounded by the internal jugular vein medially, the trapezius muscle laterally, and the clavicle and the subclavian vein caudalward, is cleared of all areolar tissue and lymph nodes The posterior belly of the omohyoid is included in the dissection At its conclusion the cords of the brachial plexus and the scaleni and levator scapulae muscles form the floor of the wound A varying number of lymph nodes, usually eight to twelve, are found in the operative specimen Care is taken to remove the nodes lying upon the venous confluence of the internal jugular and subclavian vein

At the Francis Delafield and the Presbyterian Hospitals during the period 1952–1955 a total of 110 of these supraclavicular dissections have been done Our data are shown in Table 122 Supraclavicular metastases were found in 20

Table 122 Supraclavicular Biopsies—Carcinoma of Breast
(Presbyterian Hospital and Francis Delafield Hospital, 1952–1955)

Type of biopsy	No of cases	Negative	Positive
Total no of cases of supraclavicular biopsy	110	88	22, or 20%
Supraclavicular biopsy only	7	4	3
Supraclavicular and internal mammary biopsy	103		
A Both positive			17
B Both negative		69	
C. Supraclavicular positive, internal mammary negative			2
D Supraclavicular negative, internal mammary positive		15	

per cent As I have already emphasized in discussing internal mammary biopsy, the disease in our patients has in general been comparatively advanced Dahl-Iversen's finding of occult supraclavicular metastasis in 8 4 per cent is much closer to the true frequency of occult supraclavicular metastasis in representative case series than our figure of 20 per cent In evaluating supraclavicular biopsy as a method of detecting advanced regional metastasis, it should be pointed out that we found only two patients among 103 subjected to supraclavicular as well as internal mammary biopsy, in whom supraclavicular biopsy showed metastasis when internal mammary biopsy did not In the 176 cases in Dahl-Iversen's 3rd and 4th series in which he also removed both supraclavicular and internal mammary nodes, there were only 5 cases in which metastases were found in the supraclavicular nodes but not in the internal mammary nodes These findings indicate that by the time the disease has reached the supraclavicular nodes the internal mammary nodes are usually also involved

The chief objection to supraclavicular biopsy, however, is that it is not a critical enough indication of inoperability due to extension of carcinoma along the axillary route My experience has taught me that when the nodes at the apex of the axilla—the subclavicular nodes—are involved, the disease cannot be cured

by surgery We have encountered occasional cases in which internal mammary and supraclavicular biopsy did not reveal metastasis, yet when radical mastectomy was done the nodes at the apex of the axilla were found to be involved The following case was such a one

Mrs. M R. a housewife aged 35 came to me on 10/5/54 complaining of a tumor of the left breast She had a hard, poorly delimited 6 cm. mass situated in the outer

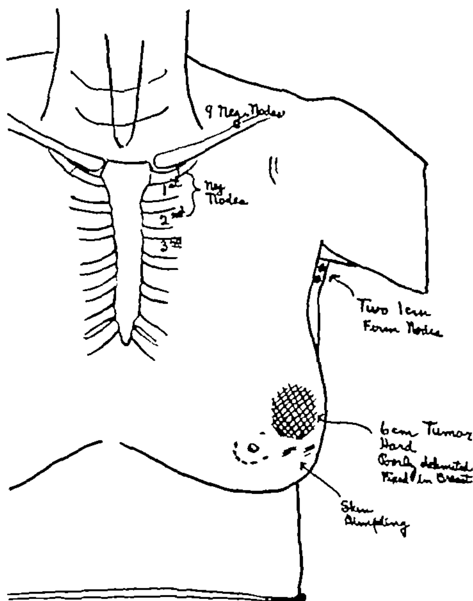


Fig 341 A patient in whom biopsy of internal mammary nodes and supraclavicular nodes failed to show *metastases. Nevertheless, the nodes at the apex of the axilla* were found to be involved when radical mastectomy was mistakenly done.

sector of the left breast (Fig 341) There were multiple lines of skin retraction below it In the axilla there were two firm nodes, somewhat fixed to the deeper structures of the axilla, each about 1 cm. in transverse diameter

From these clinical facts I suspected that this patient s disease might be inoperable and I performed a triple biopsy to confirm the diagnosis and to determine the extent of the regional metastases. The primary tumor was an undifferentiated carcinoma. Nodes obtained from the 1st. 2nd. and 3rd interspaces did not contain metastases.

Our *technique* for our supraclavicular biopsy has been the standard one for supraclavicular dissection The skin incision is an oblique one across the base of the neck The external jugular vein is sacrificed The sternocleidomastoid is retracted medially, and the triangle which is bounded by the internal jugular vein medially, the trapezius muscle laterally, and the clavicle and the subclavian vein caudalward, is cleared of all areolar tissue and lymph nodes The posterior belly of the omohyoid is included in the dissection At its conclusion the cords of the brachial plexus and the scaleni and levator scapulae muscles form the floor of the wound A varying number of lymph nodes, usually eight to twelve, are found in the operative specimen Care is taken to remove the nodes lying upon the venous confluence of the internal jugular and subclavian vein

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thoraco-acromial vessels These latter vessels should on no account be disturbed in the biopsy dissection for two reasons In the first place, the nodes to be removed are those lying medially to these vessels Secondly damage to these vessels, with hemorrhage into the area interferes with the nicety of dissection in this area if a radical mastectomy is subsequently decided upon All that is needed in the biopsy procedure is to excise the small mass of areolar tissue, together with any obvious lymph nodes, from the small area that I have described This must be done with meticulous hemostasis and without damage to the axillary vein The small mass of areolar tissue which constitutes the biopsy specimen should be placed at once in a good fixative embedded in paraffin and cut in a number of levels. Frozen sections are not adequate for the identification of the minute foci of carcinoma that may be found in a specimen of this kind

During the first ten months of 1955 we performed 41 of these apex of axilla biopsies, as shown in Table 123 In 11 or 26 8 per cent metastases were found

Table 123 Apex of Axilla Biopsies—Carcinoma of Breast
(Presbyterian Hospital and Francis Delafield Hospital, 1952–1955)

Type of cases	No of cases	Negative	Positive
Total no of cases of apex biopsy	41	30	11 or 26 8%
Axillary apex biopsy only	2	1	1
Axillary apex and internal mammary node biopsy	39		
A. Both positive			7
B Both negative		26	
C. Apex positive, internal mammary negative			3
D Apex negative, internal mammary positive		3	

In 39 of the cases the internal mammary nodes were also biopsied. The apex of axilla nodes were *involved in three cases in which internal mammary metastases* were not found.

In 8 of the patients with involvement of the highest axillary nodes there were clinically involved axillary nodes measuring 2 cm or more in diameter In one patient there was only a single clinically involved axillary node 1 cm. in diameter In the remaining two patients there were no clinically involved axillary nodes, but in both the primary tumor was 5 cm. or more in diameter In one of these the internal mammary node biopsy showed metastases but in the other patient nodes were removed from the upper three interspaces and found to be uninvolved This patient s primary tumor was situated in the upper outer sector of her breast as shown in my sketch (Fig 343) It measured 8 x 6 cm. in diameter Her disease was operable by every criterion except for the occult metastases in the nodes at the apex of her axilla.

These data suggest that biopsy of the apex of the axilla is a more critical indicator than supraclavicular biopsy of the spread of mammary carcinoma along the axillary supraclavicular route to the highest axillary nodes from which the conventional radical mastectomy cannot eradicate it We have not yet done enough apex of axilla biopsies to be able to define precisely which patients it is worth while to subject to the procedure The extent of the clinical involvement

Seven nodes removed in the supraclavicular dissection were not involved Radiographic study of the chest and the skeleton did not show metastases

Having failed to prove that the disease was beyond the reach of surgical attack, I performed radical mastectomy In dissecting the axilla I was distressed to find many small grossly involved nodes extending to the highest part of the axilla Pathological study of the operative specimen confirmed this impression Of 30 lymph nodes found, 28 contained metastases

A patient with such extensive axillary metastases has, in my experience, an exceedingly small chance of cure by surgery I believe that radiotherapy is a better method of treatment for such patients Dissection of the supraclavicular nodes for biopsy may fail, as it did in the above patient, to indicate that the disease is incurable by surgery In search of a more critical biopsy method of de-

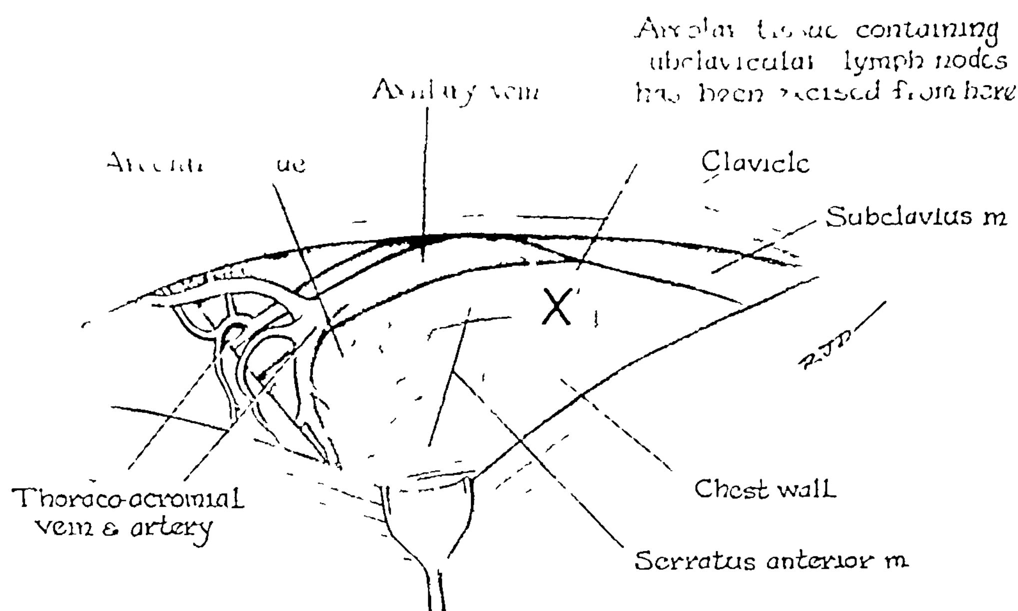


Fig 342 The apex of the axilla exposed for biopsy

termining the extent of metastatic spread along the axillary-supraclavicular route, I abandoned supraclavicular biopsy early in 1955 and began instead to biopsy the lymph nodes at the apex of the axilla

Biopsy of the Apex of the Axilla. The group of nodes which we biopsy are the so-called subclavicular nodes (see Chapter 1) which lie upon and caudad to the axillary vein just before it passes beneath the tendon of the subclavius muscle to become the subclavian vein This is the terminal portion of the axillary lymph node filter

These nodes are reached through a short 4 to 6 cm incision made about 2 cm below and parallel to the middle of the clavicle The pectoralis major muscle is split and retracted, or severed, just below its attachment to the clavicle The deep axillary fascia is exposed, the axillary vein identified, and the fascia incised caudad to it This defines a small area containing areolar tissue in which there are embedded a few small lymph nodes The area is bounded, as shown in Figure 342, cephalad by the axillary vein, medially by the subclavius tendon applied to the clavicle, below by the chest wall covered by the serrati, and laterally by the

in whom our regional lymph node biopsies do not reveal metastases I do not believe that this delay adds appreciably to the danger of distant metastases that our patients face The triple biopsy on the other hand unquestionably saves many patients from futile radical mastectomy and relegates them to the kinder sentence of radiotherapy I will discuss the value of chest wall resection and other forms of extended radical mastectomy in Chapter 27 The type of radical mastectomy to which our biopsy criteria *apply is the conventional radical mastectomy* or what we might better call the Halsted mastectomy to distinguish it from the several more extensive forms of surgical attack now being tried out

Table 124. Carcinoma of Breast Regional Node Biopsies
(Presbyterian Hospital and Francis Delafield Hospital, 1952–1955)

Types of biopsies	No. of cases	Cases with positive nodes	
		No	Per cent
A. Internal mammary and supraclavicular biopsy	102	34	33 3
B Internal mammary and axillary apex biopsy	38	13	34 2
C. Internal mammary biopsy only	163	54	33 1
D Supraclavicular biopsy only	7	3	42 9
E. Axillary apex biopsy only	2	1	50 0
F Internal mammary supraclavicular and axillary apex biopsy	1	0	0 0
Total regional lymph node biopsies	313	105	33 5

The details of our findings with triple biopsy are shown in Table 124 With this method we have found metastases in the regional lymph node filter beyond the reach of the conventional radical mastectomy in 33 5 per cent of our cases

The decrease in our operability rate resulting from these regional lymph node biopsies is indicated in Table 125 which presents our biopsy data concerning 156 Francis Delafield Hospital cases It will be seen that our former clinical criteria of operability in which the assessment of the extent of the metastases in the regional lymph node filter was based only upon palpation placed only 25 6 per cent of these 156 cases in the inoperable category With our regional lymph node biopsies, however we proved that the disease was inoperable in an additional 23 8 per cent of the cases This brought our operability rate down from 74 4 per cent to 50 6 per cent and saved 37 futile radical mastectomies When this operability rate of 50 6 per cent, to which our biopsy criteria have led us, is compared with the operability rate of 93 per cent which is current in New York State today it is obvious that we are selecting our patients for operation with great care and that we are at least part way toward the ideal which I have suggested—namely, to avoid operating upon patients who cannot be cured by the Halsted operation

A closer analysis of the reasons for classifying patients as inoperable in our Francis Delafield Hospital series of 156 cases in which regional lymph node biopsies were done is made in Table 126 Comparing the relative importance of

of the axillary nodes is certainly our best guide Any patient who has more than a single, small, involved axillary node should have the apex of her axilla biopsied

Triple Biopsy. Our search for *biopsy criteria* which will accurately determine the extent of regional lymph node metastasis and guide us in selecting patients who can be cured by operation has evolved into what my associates McDonald and Stout and I have called the *triple biopsy* This is done as a separate preliminary biopsy operative session The primary breast carcinoma is of course biopsied first After its carcinomatous nature has been proved by frozen section the biopsy

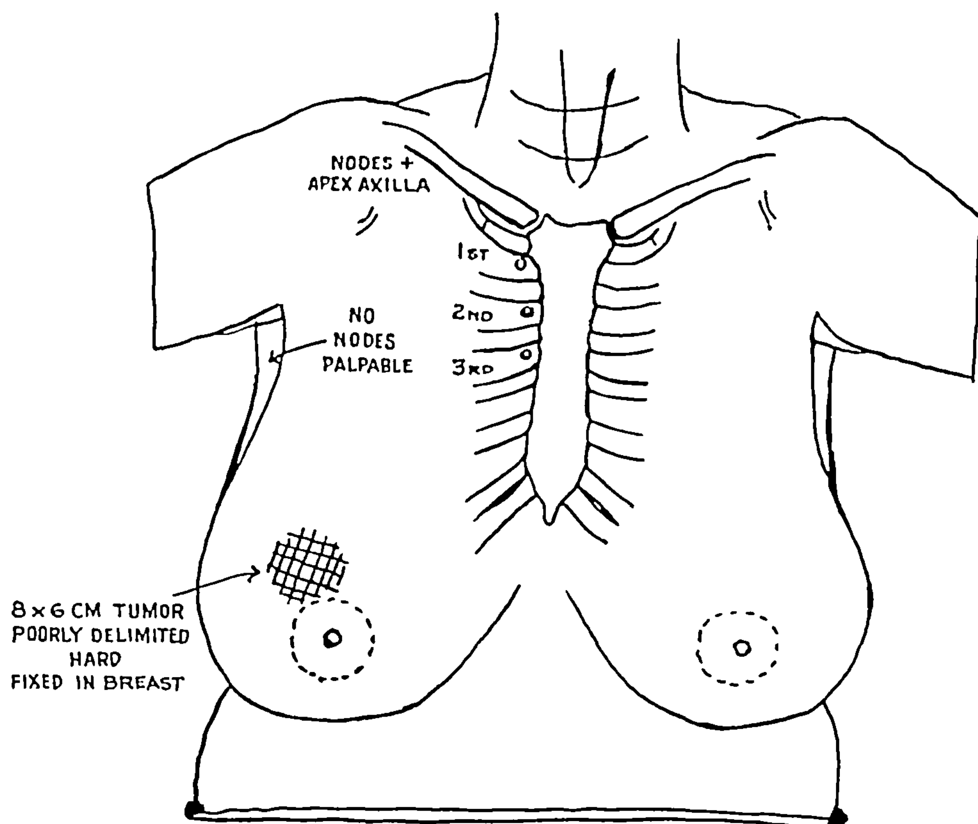


Fig 343 A patient with an 8 cm carcinoma of the upper outer zone of the breast in whom the internal mammary biopsy was negative but biopsy of the apex of the axilla revealed metastases

wound is carefully sutured and sealed off with a generous piece of rubber dam cemented over it Instruments, gowns and gloves are then changed, and the upper three interspaces explored according to the technique which I have described above This parasternal incision is then sutured and sealed off

Again, instruments, gowns and gloves are changed and the third portion of the triple biopsy carried out This was formerly a supraclavicular dissection, but is now biopsy of the apex of the axilla

It is of course impractical to perform such triple biopsies in every patient with breast carcinoma But we attempt to carry them out on all patients in whom the clinical findings are suggestive of the presence of metastases in the internal mammary area or the apex of the axilla

This plan necessitates a delay of from three or four days to a week in carrying out radical mastectomy at a separate subsequent operative session upon patients

inoperable and regional node biopsy was not justified In the remaining 28 in whom the disease was operable, regional node biopsy was not done for a variety of reasons, usually because the carcinoma appeared to be early and clearly operable. This group of 106 patients who did not have regional node biopsy is not of much assistance to us in studying criteria of inoperability The disease in most of them was too far advanced

It is interesting however to compare our classification of patients as to inoperability in our older Presbyterian Hospital series of cases in which judgment as to operability was based upon *clinical criteria* with our classification of our recent series of Francis Delafield Hospital cases based upon *regional node biopsy criteria.*

Table 127 Operability in 1544 Patients with Breast Carcinoma Who Did Not Have Regional Lymph Node Biopsies
(Presbyterian Hospital, 1915–1942)

Basis for judgment as to operability			No. of patients	Per cent
Clinical criteria	*Involved supraclavicular nodes or parasternal mass*	*Distant metastases*		
A. Operable	Operable	Operable	1133	73 4
B. Inoperable	Operable	Operable	200	13 0
C. Operable	Inoperable	Operable	18	1 2
D Operable	Operable	Inoperable	58	3 8
E. Inoperable	Inoperable	Operable	38	2 5
F Inoperable	Operable	Inoperable	9	6
G Operable	Inoperable	Inoperable	55	3 6
H. *Inoperable*	*Inoperable*	*Inoperable*	*33*	2 1
Total no inoperable cases			411	26 6
Total no cases classified			1544	100

Table 127 shows the 1544 Presbyterian Hospital cases (1915–1942) classified as to operability When the data in this table are compared with those in Table 126 it is obvious that our former clinical criteria were much less critical, and that their great defect lay in the fact that they failed to detect disease in the regional lymph node filter With our former clinical criteria this stage was recognized only when the supraclavicular lymph nodes became palpable or there was a parasternal tumor

Table 128 shows the older Presbyterian Hospital series of cases as well as our recent Francis Delafield Hospital series of cases classified as to operability by the different criteria The greater critical value of our biopsy method of classification is well shown. The closeness of the findings in categories A and B in the two series should be noted This similarity suggests that if regional lymph node biopsies (Category C) had been done in the Presbyterian Hospital series of cases, metastases would have been found as frequently as in our Francis Delafield Hospital series of cases. If this assumption is true approximately 350 futile radical mastectomies would have been avoided in the older Presbyterian Hospital series of cases by regional lymph node biopsies such as we do today

the three different types of criteria that enter into our judgment as to operability —(1) *clinical criteria* as to the extent of the disease locally and in regional lymph nodes, (2) *regional lymph node biopsies* and (3) *x-ray and biopsy search for distant metastases*—it is seen that regional lymph node biopsy had the largest role in

Table 125. Alterations in the Rate of Operability Resulting from Regional Lymph Node Biopsies
(Francis Delafield Hospital, 1952–1955)

	Patients undergoing regional node biopsy
No of patients	156
No inoperable by *local clinical criteria*	27
No inoperable because of distant metastasis	13
Operability rate based on the clinical criteria only	74 4%
Number of patients found inoperable by regional lymph node biopsy	37
Actual number of radical mastectomies	79
Actual operability rate based on clinical and biopsy criteria	50 6%
Decrease in operability rate resulting from regional node biopsies	23 8%

Table 126 Operability of 156 Patients with Breast Carcinoma Receiving Regional Node Biopsy
(Francis Delafield Hospital, 1952–1955)

Basis for judgment as to operability			Number of patients	Per cent of patients
Clinical criteria	Regional node biopsies	Distant metastases		
A Operable	Operable	Operable	79	50 6
B Inoperable	Operable	Operable	12	7 7
C Operable	Inoperable	Operable	37	23 7
D Operable	Operable	Inoperable	3	1 9
E Inoperable	Inoperable	Operable	15	9 6
F Inoperable	Operable	Inoperable	1	0 6
G Operable	Inoperable	Inoperable	8	5 1
H Inoperable	Inoperable	Inoperable	1	0 6
Total number of inoperable cases			77	49 4
Total number of cases classified			156	100

revealing inoperability Approximately one-half of the cases that were finally classed as inoperable were proved to be so *solely* by regional lymph node biopsy

This analysis of our basis for judging operability in our Francis Delafield Hospital breast carcinoma cases does not take into account 106 cases in which regional biopsy was not performed In 78 of them the disease was obviously

ment is decided upon They have revealed distant metastases in about 10 per cent of our patients

Unfortunately as I have pointed out in Chapter 19 x ray study is a crude and inaccurate method of demonstrating metastases Over and over again x ray study fails to reveal metastases, yet they become evident within a year or two after radical mastectomy Such metastases were undoubtedly present at the time of operation We greatly need more efficient methods of demonstrating occult metastases in the bones and viscera.

At the Francis Delafield Hospital during the last few years we have been attempting to develop new methods of demonstrating metastases in bones We first studied the usefulness of bone marrow aspiration utilizing the crest of the ilium The smears made from the aspirated material were prepared as blood smears and studied by our hematologist and pathologist Hyman has recently summarized our results with this method It did not achieve as high a degree of accuracy as we had hoped For example, in a series of 41 patients in whom skeletal metastases from breast carcinoma were demonstrated radiographically aspiration of the iliac crest revealed carcinoma cells in only 10

Trephine Biopsy A method of trephine biopsy developed in the Francis Delafield Hospital by Dr Wolfgang Ackermann has however proved much more successful It has been used chiefly for biopsying the lower vertebrae, which are, of course the commonest site of osseous metastases Dr Ackermann secures, with this method a perfectly adequate cylinder of vertebral marrow This is fixed and sectioned like any tissue specimen Figure 344 shows such a biopsy specimen from a lumbar vertebra containing metastatic mammary carcinoma.

Dr Ackermann's description of his method, summarized from his recent paper follows.

Instruments None of the available bone trephine instruments were satisfactory and new ones had to be designed The construction of the instruments was turned over to an instrument manufacturer in this particular field. Stainless steel was used for the construction of all parts, with the exception of the Luer attachments which are chrome plated After some initial improvements the final set was completed It is composed of

1 PERFORATOR (Fig. 345 *B* and *C*) It has an over all length of 4 5 cm Its top is a 3 mm. thick, flat, solid, round and knurled disc 18 mm. in diameter its solid shaft, which is 2 5 mm. in diameter ends with a 1 cm. long, three-edged, sharp pointed cutting tip The perforator serves for cutting skin and dense fasciae down to the muscles It does it with ease causing hardly any bleeding, unlike the knife customarily used.

2 LOCATOR (Fig 345 *D*) It has an over all length of 15 cm Its shaft is 2 mm in diameter Its top is like that of the perforator but its 1 cm long tip which gradually narrows down to a dull point, has a smooth surface.

3 TREPHINE GUIDE (Fig 345 *D*) It is a tube with an over all length of 14 cm. At its upper end is a 15 mm. long Luer needle hub to be used if additional Novocain to anesthetize the periosteum is needed The outer surface of the tube beginning at 4 cm. from the lower end is graduated in 1 cm. intervals up to 10 cm Its outside diameter is 2.5 mm and its inner diameter readily admits both the locator and the trephine.

A final method of determining the comparative value of our *clinical criteria* of operability and our *regional node biopsy criteria* is an analysis of the basis for classification as to operability of all the patients in whom we have performed regional node biopsy during the last four years They totaled 313, and are shown

Table 128. Comparative Value of *Clinical* and *Regional Node Biopsy* Criteria of Operability in Breast Carcinoma

Criteria of operability	Presbyterian Hospital 1915–1942		Delafield Hospital 1952–1955	
	Inoperable category		Inoperable category	
	No of patients	Per cent	No of patients	Per cent
A Distant metastases evident	155	10 0	13	8 3
B Clinical criteria (no evidence of distant metastasis)	238	15 4	27	17 3
C Regional node biopsy (no other signs of inoperability)	18	1 2	37	23 7
Total no inoperable cases	411	26 6	77	49 4
Total no cases classified	1544		156	

Table 129. Comparative Value of *Clinical* and *Regional Node Biopsy* Criteria in Breast Carcinoma

(Presbyterian and Francis Delafield Hospitals, 1952–1955)

Operability as shown by		No of patients	Per cent
Clinical criteria including distant metastasis	Regional node biopsy		
A Operable	Inoperable	74	60 4
B Inoperable	Inoperable	31	9 9
C Inoperable	Operable	19	6 1
Total no inoperable cases		124	39 6
Total no cases classified		313	100 0

in Table 129 One hundred and twenty-four cases were classified as inoperable In 60 4 per cent the judgment as to inoperability was based entirely on the finding of metastases in the regional nodes This single fact is adequate proof of the value of regional lymph node biopsy

*4. **Distant Metastases Related to Operability.*** No one would deny that the demonstration of distant metastases in carcinoma of the breast is a contraindication to radical mastectomy Yet a great many women are operated upon who have them I cannot excuse a surgeon who performs radical mastectomy without having had roentgenograms of the chest and bones, searching for metastases In our hospitals these x-ray studies have regularly been carried out before treat-

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Criteria of operability	Presbyterian Hospital 1915–1942		Delafield Hospital 1952–1955	
	Inoperable category		Inoperable category	
	No. of patients	Per cent	No. of patients	Per cent
A. Distant metastases evident	155	10.0	13	8.3
B. Clinical criteria (no evidence of distant metastasis)	238	15.4	27	17.3
C. Regional node biopsy (no other signs of inoperability)	18	1.2	37	23.7
Total no. inoperable cases	411	26.6	77	49.4
Total no. cases classified	1544		156	

Table 129. Comparative Value of *Clinical* and *Regional Node Biopsy* Criteria in Breast Carcinoma

(Presbyterian and Francis Delafield Hospitals, 1952–1955)

Operability as shown by: Clinical criteria including distant metastasis	Operability as shown by: Regional node biopsy	No. of patients	Per cent
A. Operable	Inoperable	74	60.4
B. Inoperable	Inoperable	31	9.9
C. Inoperable	Operable	19	6.1
Total no. inoperable cases		124	39.6
Total no. cases classified		313	100.0

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motion The outside diameter of the trephine is 2 mm and its inner diameter is 1.5 mm. Its tip has a serrated edge and it represents a circular saw with six very fine sharp teeth beveled on the leading edge for cutting The inner bore is straight to permit easy advancement of the core like specimen up the trephine

The long trephine is exactly the same as the short one except that it is 1 25 cm longer Thus it has an over all length of 18 cm

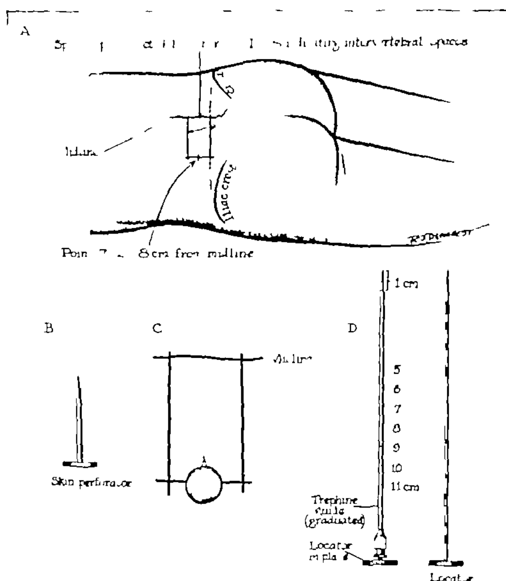


Fig. 345 Trephine biopsy

A landmarks of L-4 to be biopsied. *B* perforator with its 3-edged tip *C* perforator in situ. *D* locator without and with trephine guide combined as a unit, with graduations in centimeters, and a 1 cm. long smooth tip

5 TWO EXTRUDERS (Fig 346 *D*) One is short and the other long. They actually are stylets for the corresponding trephines with the sole purpose of extruding the specimens They too are topped with knurled disks, which are 7 mm in diameter reinforced to facilitate expelling of the specimens

Technique On May 12, 1954 the first vertebral trephine biopsy was performed on a patient. It was carried out in the Department of Radiology on an x ray

The purpose of the locator is to direct the trephine guide to the area to be biopsied When the locator is completely inserted into the trephine guide, both are combined as a unit, and as such the unit is inserted into the opening made in the skin by the perforator

When in use as a unit the 1 cm long tip of the locator protrudes beyond the trephine guide Because of its dull point, it can easily advance the unit forward



Fig 344 Trephine biopsy of lumbar vertebra showing metastatic carcinoma

through muscles and thin fasciae, but not through nerves or blood vessels, which are not injured by the non-cutting instruments if limited force is applied

4 TWO TREPHINES (Fig 346 *B*) One is short and the other long The short trephine is a tube with an over-all length of 16 75 cm At its upper end is a Luer needle-hub, for eventual bone marrow aspiration Below the needle-hub is a knurled disk This disk has the same dimensions as the disk of the perforator and the locator While the disk of the perforator and locator serve to facilitate their insertion, the trephine disk is used to facilitate cutting into the bone by a rotating

the margins of both iliac crests This line passes either over the body of L-4 or, as it does most of the time, over the fourth interspace between L-4 and L 5

4 A line is drawn along the midline over the lumbar spinous processes down to the sacrum

The left side of the patient is routinely preferred for the biopsy because on the left the aorta is situated more anteriorly than the vena cava on the right There is therefore less chance of injuring the aorta when the left side is used than of injuring the vena cava when the right side is used There is also the fact that the right kidney being topographically lower than the left can be more easily damaged.

5 Lines are drawn along the interspaces above and below the vertebra to be biopsied These lines which are parallel to each other extend from the midline laterally for a distance of 8 cm except in patients who weigh 100 pounds or less in whom a distance of only 7 cm is used The lateral ends of these parallel lines are then connected by a perpendicular line, and at its center a cross is marked This is the entrance point for the nerve block as well as for the perforator

6 The skin of the back is prepared as for any other operation and the area is draped

7 At the cross mark a skin wheal is followed by a paravertebral nerve block with 10 to 15 ml of 1 per cent Novocain without adrenalin if only one vertebra is biopsied In the nerve block the posterior root must be included because a branch of it supplies the periosteum the most sensitive structure involved in this operation, as well as the bone proper

8 Immediately upon completion of the paravertebral block the perforator is introduced at the cross mark through the skin and thick fasciae down to the muscles for a depth of 3 cm

9 The locator together with the trephine guide as a unit, is inserted through the track thus established, and advanced medially and downward at an angle of about 45 degrees until the body of the vertebra is encountered usually at a depth of 8 to 9 cm In emaciated people the distance is 6 to 7 cm

10 The point of the locator is bored into the cortex of the vertebra to make it stay in place for the radiographic check

11 Roentgenographs in AP and lateral views are taken, and the position of the instruments checked in the wet films If unlike those in Fig 347 their position does not appear satisfactory the necessary adjustment is made The locator can easily be swung up or down forward or backward changing the angulation to a more or less acute bend. The topographical relations of the instrument to the nerve roots as well as to the large vessels must always be kept in mind.

12. The trephine guide, which in the unit is 1 cm shorter than the locator is advanced for that distance and brought into contact with the vertebral body It is held fast in that position by the left index finger and thumb

13 The locator is removed and replaced by the short trephine which is brought into contact with the vertebral body With gentle pressure, the trephine is slowly driven through the periosteum and cortex and into the marrow (Fig. 348) by rotation of its knurled disk

14 Roentgenographs are taken in two views for the second time The wet films are again checked for the exact location as well as for the angulation of

table and under a Novocain-block anesthesia No difficulties of any kind were encountered The procedure has since undergone a number of modifications At present the technique is being performed as follows

1 One-half hour before the operation takes place the patient receives an intramuscular injection of 100 mg of Demerol for sedation

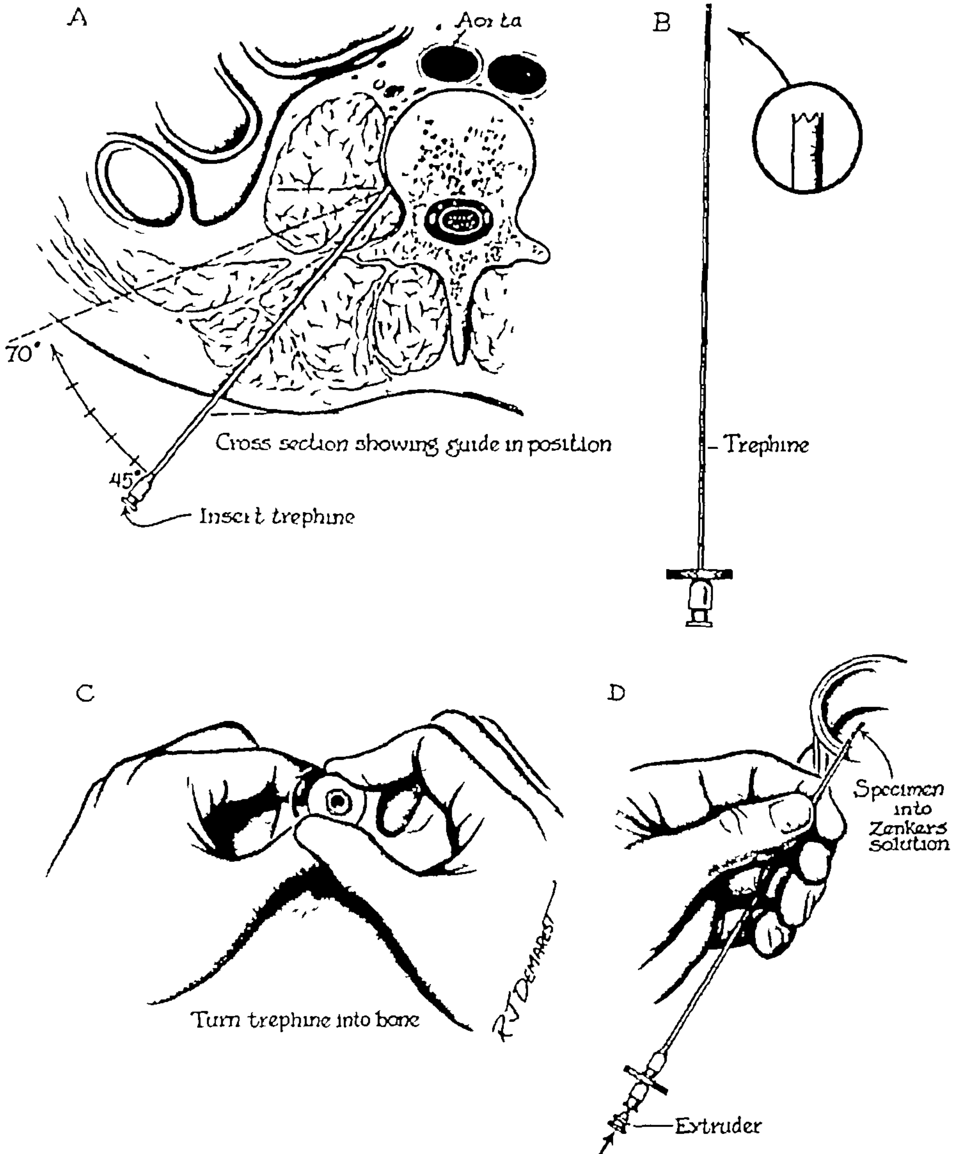


Fig 346 Trephine biopsy

A, angulation range of the trephine guide on a cross section *B*, trephine and its serrated tip (insert) *C*, trephining procedure *D*, inspection of extruded specimens prior to placing in Zenker's solution

2 Immediately upon arrival in the Roentgenologic Department the patient is placed on the x-ray table in the prone position, with an extra pillow under the lower abdomen so that the spinous interspaces are widened and the landmarks more easily established (Fig 345 *A*)

3 With a dermatograph a line is drawn across the lower back at the level of

the trephine Figure 349 shows the trephine driven about half way in the body of L 3

15 The trephine is now rotated several times clockwise, without dislodging it, in order to break off the core like specimen The trephine is then withdrawn with continuous slow rotating motion

16 The trephine guide, still being in contact with the vertebral body is now adjusted as to the most desired angulation The long trephine is then introduced through both the guide and through the track cut by the short trephine through the cortex, and bored into the vertebra to its full length

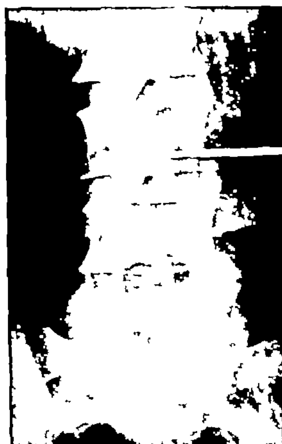


Fig. 349 The trephine driven about half way into the body of L3 (AP view)

Because the long trephine cuts more deeply into the vertebral marrow than the short trephine it obtains a specimen not only from a different location but also at a different depth This second specimen has therefore less cortical bone and more marrow

17 The long trephine is now left in place, and by means of the extruder the specimen from the short trephine is expelled (Fig 346 *D*) Before it is placed in the bottle of Zenker s solution it is observed as to its color and general appear ance to ascertain the amount of marrow present

18 Long trephine is removed and the specimen is expelled from it by the extruder and its characteristics observed

This procedure of obtaining two specimens can if necessary be repeated once or twice on the same vertebra either above or below the area just biopsied thus

Fig 347. The end of the tip of the locator is bored into the cortex of L-3, just below its central part

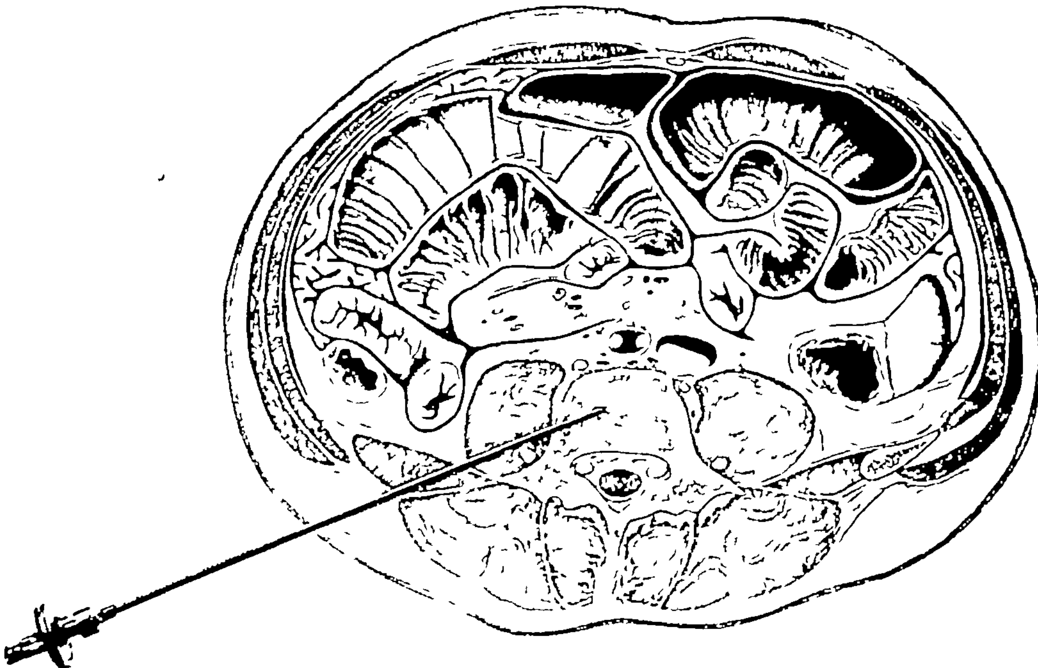


Fig 348 Cross section through the lower portion of the fourth lumbar vertebra Short trephine is down to its full length deep in the marrow of L-4, while the trephine guide is still in place Observe the thickness of the lumbar aponeurosis, also the absence of the kidneys (Courtesy Eycleshymer and Shoemaker, Cross-Section Anatomy, 4/5 natural size, D Appleton Company)

roentgenographic evidence of metastases in the vertebrae which were biopsied Trephine biopsy revealed carcinoma in all five Trephine biopsy revealed metas tases in 4 additional patients who had neither roentgenographic evidence of a vertebral lesion nor pain suggesting its presence

Our experience with the trephine biopsy method convinces us that it should be used whenever pain suggests bone metastases as well as in those cases in which the radiographic evidence is only suggestive or indeterminate By means of it the presence of metastases can be confirmed and the patient spared a futile radical mastectomy

Trephine biopsy can also be of value in ruling out vertebral metastases, thereby saving the patient from unnecessary radiotherapy There is an infrequent non neoplastic lesion of the vertebrae characterized by the development of a dense area of sclerosis in the vertebral body These lesions are usually single and fairly large They are situated contiguous to the edge of the vertebrae Their etiology is unknown but in several instances they have been associated with disk disease When they occur in a patient who has breast carcinoma they naturally suggest the osteoblastic type of metastasis If there is any clinical reason to doubt this diagnosis, trephine biopsy should be done A recent experience with a patient of mine illustrates this point.

The patient had had a breast carcinoma without axillary metastases operated upon 13 years previously She returned complaining of lower back pain In her x ray films a single area of increased density was seen in the body of the 2nd lumbar vertebra This was diagnosed by the roentgenologist as metastasis. Fortunately for the patient we were doubtful of the nature of the vertebral lesion, first because her carcinoma had been a favorable one operated upon long ago and secondly because of its x ray appearance. A trephine biopsy revealed only sclerotic bone with no evidence of meta stasis

Summary

The choice of treatment for breast carcinoma resolves itself for me not in the use of any one method of treatment for all cases, but in the selection of the appropriate form of treatment for each stage of the disease When the disease is as yet of comparatively limited extent locally and in the axillary lymph nodes the Hal sted radical mastectomy is the best treatment When the disease has extended farther in the regional lymph node filter and involved the internal mammary nodes, or the nodes at the apex of the axilla or those in the supraclavicular region I have chosen to rely upon irradiation rather than surgery New and more extensive methods of surgical attack upon this stage of the disease are being currently tested but their value is as yet not proved Operation does harm when it is used upon patients whom it cannot cure All such patients are better treated by irradiation *My aim is not to operate upon patients whom I cannot cure*

The problem of accurately estimating the extent of the carcinoma in the indi vidual patient in order that the right treatment can be chosen is therefore the crucial one Our study of the significance of a variety of clinical signs of the extent of the disease in terms of the possibility of cure by surgery led us to draw up a list of clinical criteria of operability These *clinical criteria* have been helpful in avoiding futile radical mastectomy for a proportion of our patients The clini

giving the pathologist specimens not only from different depths but also from different levels

Since metastases in bones are nearly always multiple, it may be desirable to biopsy more than one vertebra If the second vertebra to be biopsied is adjacent to the first one, the procedure is carried out from the same entrance point by directing the instruments upward or downward at an acute angle in relation



Fig 350 By swinging the trephine guide alone or in combination with the locator tip up or down, from the same entrance point, two, or even three vertebrae can be biopsied at one operation

to the midline (Fig 350) This maneuver must, of course, be preceded by a nerve block of the corresponding root

This method has been used by Ackermann to biopsy the vertebrae in 147 patients in the Francis Delafield Hospital There were no injuries or complications in these patients They were selected at random from patients with proved carcinoma without regard to the presence of clinical or x-ray indications of bone metastases Seventy-five of the patients had breast carcinoma Five of these had

roentgenographic evidence of metastases in the vertebrae which were biopsied Trephine biopsy revealed carcinoma in all five Trephine biopsy revealed metastases in 4 additional patients who had neither roentgenographic evidence of a vertebral lesion nor pain suggesting its presence

Our experience with the trephine biopsy method convinces us that it should be used whenever pain suggests bone metastases as well as in those cases in which the radiographic evidence is only suggestive or indeterminate. By means of it the presence of metastases can be confirmed and the patient spared a futile radical mastectomy

Trephine biopsy can also be of value in ruling out vertebral metastases thereby saving the patient from unnecessary radiotherapy There is an infrequent non neoplastic lesion of the vertebrae characterized by the development of a dense area of sclerosis in the vertebral body These lesions are usually single and fairly large They are situated contiguous to the edge of the vertebrae Their etiology is unknown, but in several instances they have been associated with disk disease When they occur in a patient who has breast carcinoma they naturally suggest the osteoblastic type of metastasis If there is any clinical reason to doubt this diagnosis, trephine biopsy should be done A recent experience with a patient of mine illustrates this point

The patient had had a breast carcinoma without axillary metastases operated upon 13 years previously She returned complaining of lower back pain In her x-ray films a single area of increased density was seen in the body of the 2nd lumbar vertebra This was diagnosed by the roentgenologist as metastasis Fortunately for the patient we were doubtful of the nature of the vertebral lesion, first because her carcinoma had been a favorable one operated upon long ago and secondly because of its x ray appearance. A trephine biopsy revealed only sclerotic bone with no evidence of metastasis.

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e in whom any of the *five grave signs* of locally advanced disease are present

8 When distant metastases are demonstrated
   a. by roentgenographic study of the chest
   b by palpation of the liver
   c. by roentgenographic search for metastases in the skeletal system
   In patients with pain in the back or pelvic area suggesting vertebral metastases trephine biopsy of the lumbar vertebrae is performed

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cal criteria have had an important defect, however, in that they fail to detect metastases in the regional lymph node filter which are incurable by the Halsted mastectomy We believe that we have solved this problem by biopsy of the internal mammary lymph nodes in the first three interspaces, and the lymph nodes at the apex of the axilla These biopsies are done at a separate preliminary operative session for the purpose of determining operability In this manner we substitute microscopical evidence for the relatively inaccurate evidence of physical examination

Our present criteria of operability, which might be called *biopsy criteria* rather than *clinical criteria* of operability, follow

Biopsy Criteria of Operability

Carcinoma of the breast in women of all age groups, who are in good enough general condition to withstand operation, should be treated by the Halsted radical mastectomy except as follows

1 When extensive edema of the skin over the breast (more than one-third of the skin area) is present
2 When satellite nodules are present in the skin over the breast
3 When the carcinoma is the inflammatory type
4 When any two, or more, of the following grave signs of locally advanced carcinoma are present
   a Ulceration of the skin
   b Edema of the skin of limited extent (less than one-third of the skin over the breast)
   c Solid fixation of the tumor to the chest wall
   d Axillary lymph nodes measuring 2 5 cm or more, in transverse diameter
   e Fixation of axillary lymph nodes to the skin or the deep structures of the axilla
5 When there is edema of the arm
6 When palpable supraclavicular nodes are present and biopsy shows metastases
7 In patients in whom biopsy of the internal mammary nodes in the 1st, 2nd, or 3rd interspaces, and/or at the apex of the axilla, reveals metastases

   Internal mammary biopsies are done for patients
   a in whom the primary tumor is situated in the lower parasternal zone of the breast (zone D)
   b in whom the primary tumor measures more than 3 cm in diameter
   c in whom any of the five *grave signs* of locally advanced carcinoma are

e in whom any of the *five grave signs* of locally advanced disease are present.

8 When distant metastases are demonstrated
   a by roentgenographic study of the chest
   b by palpation of the liver
   c. by roentgenographic search for metastases in the skeletal system
   In patients with pain in the back or pelvic area, suggesting vertebral metastases, trephine biopsy of the lumbar vertebrae is performed

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CHAPTER 27

THE SURGICAL TREATMENT OF MAMMARY CARCINOMA

In the preceding chapter I have described the method by which we select the Halsted radical mastectomy as the treatment for about one half of the patients who come for treatment of primary carcinoma of the breast The operation itself is an extensive one in which a series of related regional dissections are integrated to form an orderly comprehensive attack upon the local disease It is an operation that cannot be improvised Depending upon science rather than art, it is more like a carefully planned military campaign than the painting of a picture. The best introduction to the operation is a review of its evolution Its development has followed step by step the advances in our knowledge of surgical pathology and the natural history of mammary carcinoma. The best historical review of the evolution of this knowledge was written by Sir D Arcy Power More recently good reviews have been made by Cooper by Craig and Holman and by Lewison

The History of the Surgical Attack upon Breast Carcinoma

Local Excision of the Tumor—Up to 1867 A hundred years ago in 1853 to be exact, Sir James Paget, one of the foremost surgeons of his time, and a great authority on breast cancer wrote I am not aware of a single clear instance of recovery that is as that the patient should live for more than ten years free from the disease In deciding for or against the removal of a cancerous breast in any single case we may I think dismiss all hope that the operation will be the final remedy for the disease Operation for breast cancer in Paget s time was merely a palliative procedure It was a simple local removal of the clinically obvious primary tumor in the breast, together with a margin of the surrounding mammary gland. It was crudely done, with much loss of blood, and was often followed by wound infection, and sometimes by septicemia as Dr John Brown described it so poignantly in "Rab and his Friends

Removal of the Entire Breast and the Axillary Lymph Nodes—1867–1875 The second stage in the development of the surgical attack on breast cancer was the removal of the entire breast rather than only a part of it, together with the axillary lymph nodes Charles H Moore, Surgeon to the Middlesex Hospital, and in charge of its cancer wards formulated this new principle of attacking breast cancer in 1867 He maintained that recurrence of the disease after the type of operation which had previously been done was not due to the develop-

ment of an entirely new tumor on the basis of a constitutional susceptibility, as was then generally considered to be the case, but to incomplete removal of the original primary carcinoma He wrote, with wisdom far beyond his time, as follows

"It is not sufficient to remove the tumour, or any portion only of the breast in which it is situated, mammary cancer requires the careful extirpation of the entire organ

"The situation in which the operation is most likely to be incomplete is at the edge of the mamma next the sternum

"When any texture adjoining the breast is involved in or even approached by the disease, that texture should be removed with the breast This observation relates especially to skin, to lymphatics, to much fat, and to pectoral muscle The attempt to save skin which is in any degree unsound is of all errors perhaps the most pernicious, and whenever its condition is doubtful, that texture should be freely removed

"In the performance of the operation it is desirable to avoid, not only cutting into the tumour, but also seeing it No actually morbid structure should be exposed lest the active microscopic elements in it should be set free and lodge in the wound Diseased axillary glands should be taken away by the same dissection as the breast itself, without dividing the intervening lymphatics, and the practice of first roughly excising the central mass of the breast and afterwards removing successive portions which may be of doubtful soundness, should be abandoned Only by deliberately reflecting the flaps from the whole mamma, and detaching it first at its edge, can the various undetected prolongations of the tumour and outlying nodules be included in the operation "

Moore's ideas were not generally accepted, although during the next decade two of his compatriots began to do the operation he had described One was Joseph Lister, then at Glasgow The other was Mitchell Banks of Liverpool Banks deserves special credit for making a vigorous plea in 1878 and again in 1882 for the removal of the axillary lymph nodes In the latter paper he wrote

"In the present paper a principal object is to advocate the removal of the axillary glands as well as the breast in *all* cases, whether we can feel them enlarged or not—in fact, to make a clearing out of the axilla a necessary part of the operation for removal of the breast I have been quietly practising this for three or four years, having been driven to the conclusion that it was the right thing to do by discovering that even in those cases where certain glands could distinctly be felt enlarged when the axilla was opened small ones were discovered which although now palpably affected, were quite incapable of being felt from th

clean its fibers just as I would in making a class room dissection carrying the knife parallel with the fibers of the muscle and penetrating the interstices The pectoralis fascia is thus entirely removed I was led to adopt this method because microscopical examination showed repeatedly what I had not expected that the fascia was already carcinomatous, whilst the muscle was certainly not involved

In Philadelphia Samuel W Gross was performing the same operation as Volkmann In his book *Tumors of the Mammary Gland* published in 1880 which was certainly the best treatise on breast tumors that had been written up to that date Gross wrote Within the past seven months, however I have adopted the principles which I have just enunciated that is to say I removed the mamma and its coverings bodily dissected off the pectoral fascia and cleaned out the axilla in five cases, and all recovered

The Modern Radical Mastectomy—1882– The final step in the evolution of the operation which we today call radical mastectomy was made by William Stewart Halsted that heroic figure in modern surgery at Johns Hopkins in 1882. That was the year in which to quote his own words, I began not only to typically clean out the axilla in all cases of cancer of the breast but also to excise in almost every case the pectoralis major muscle or at least a generous piece of it, and to give the tumor on all sides an exceedingly wide berth Halsted s first description of his operation as he had performed it in 13 cases of carcinoma of the breast, was published for the first time in 1891 in a section of a paper on "The Treatment of Wounds

Although Halsted had received his medical education in New York he had spent much time in Germany and was fully aware of Volkmann s surgical ideas and of the facts concerning the lymphatic spread of carcinoma as they were emerging in several German laboratories

Halsted was not only prepared intellectually to advance the new concept of a truly radical surgical attack upon carcinoma of the breast but he was technically prepared to carry out the concept. He was a pioneer in the development of precise meticulous surgical dissection, using small hemostats and silk ligatures He was one of the few surgeons of his day who had mastered the technique of grafting skin, which permitted him to remove as much tissue as he wished from the chest wall and still close his wound without tension All these features of his technique made it possible for him to carry out the extensive dissection which his concept of the treatment of breast carcinoma required and still achieve good wound healing.

Halsted wrote four papers presenting his concept of the surgical attack on breast cancer and his results They were published in 1894 1898 1907 and 1912. They should all be read by every student of breast cancer In his first paper in 1894 Halsted reviewed the results of earlier and less radical operations in the hands of German, French and American surgeons, and pointed out the incompleteness of these earlier operations He then described his own operation, as it had evolved in his hands, emphasizing a cardinal principle that the suspected tissue should be removed in one piece (1) lest the wound become infected by the division of the tissues invaded by the disease or of lymphatic vessels containing cancer cells, and (2) because shreds or pieces of cancer tissue might readily be overlooked in a piecemeal extirpation He included brief reports of the 50 rad

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ical mastectomies which he had performed to date without a single operative death

During the same month of November, 1894, that Halsted's first paper appeared in print, Willy Meyer of New York, read before the New York Academy of Medicine, Section on Surgery, a description of a technique for radical mastectomy which was similar to Halsted's At the time he described his operation, Willy Meyer had performed it on six patients during the previous three years

There is no doubt that Halsted and Willy Meyer conceived the radical mastectomy independently, but for history it must be pointed out that Halsted began to do his operation in 1882, while Willy Meyer first performed his operation in 1891

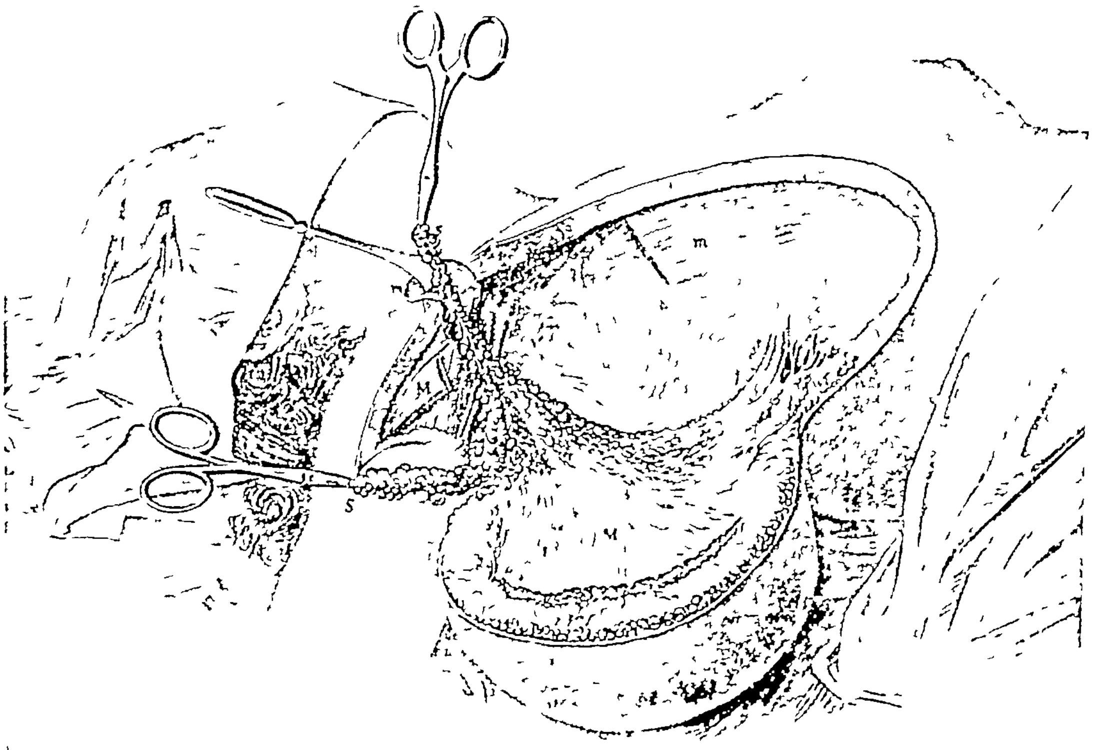


Fig 351 Halsted's original illustration showing the operative specimen at the patient's side as he dissects the axilla

Although the Halsted and Willy Meyer operations were similar in scope there were important differences in the manner in which the two procedures were carried out Halsted detached the pectoralis major muscle with the overlying breast from the sternum and the chest wall as soon as he had dissected back his skin flaps The operative specimen then was permitted to fall laterally, giving good access to the axilla which was dissected last Halsted's original illustration shows the operative specimen at the patient's side as he dissects the axilla (Fig 351) In Willy Meyer's operation the axilla was dissected first This step being completed, the operative specimen was retracted medially, the deep surface of the pectoral muscles being exposed as their attachments to the chest wall and the sternum were severed Strong retraction was required during this step, a feature better avoided in a cancer operation Willy Meyer's illustration (Fig 352) shows

this maneuver Halsted merely divided the pectoralis minor muscle and left it in situ while Willy Meyer removed it Another difference between the two operations was that Halsted regularly sacrificed so much skin over the breast that it was necessary to cover the defect on the chest wall with a graft Willy Meyer sacrificed less skin and was often able to close his wound without grafting

An important advantage of Halsted s operation was that it was a more precise careful dissection carried out with meticulous hemostasis and requiring about four hours to complete The access to the axilla when axillary dissection



Fig. 352. Willy Meyer s original illustration showing the operative specimen being retracted medially as the pectoral muscle is detached from the chest wall in the last stage of the operation

was performed as a last stage with the breast out of the way at the patient s side was excellent, and permitted gentle, accurate sharp dissection Willy Meyer s operation was done more rapidly requiring only about two hours, and was bloodier and rougher The access to the axilla, which was dissected before the breast was removed from the chest wall was not good The axillary dissection was done bluntly with a scalpel handle or closed scissors or a gauze mop

As time went by both Halsted and Willy Meyer modified their techniques somewhat Halsted shortly adopted excision of the pectoralis minor muscle For many years he included a supraclavicular dissection as part of his operation but finally gave this feature up as futile About 1910 he made a final important tech

nical improvement in his skin incision. He abandoned the incision extending out onto the arm, and carried his incision straight upward from his circular incision around the breast to the strap line at the center of the shoulder. This avoided disfigurement of the axilla and upper arm by an unsightly scar.

Both of these operations were welcomed and quickly accepted in this country. Halsted's operation was performed chiefly by his pupils, however, and has never been widely practiced. Willy Meyer's operation was adopted more widely. Warren, in Boston, took it up and modified the skin incision slightly. Jackson, of Kansas City, introduced the operation in the middle west, with another modification of the skin incision. Rodman, in Philadelphia, devised still another skin incision. It was the Willy Meyer operation, not the Halsted operation, which has evolved into what may be called the "standard American radical mastectomy," which is practiced throughout most of the world today. This is a quicker, less meticulous, more brutal operation than the original Halsted operation. Skin grafting is rarely done. To avoid it, less skin is sacrificed, and the wound is put together with considerable tension.

The effects of the Halsted and Willy Meyer operations upon results in carcinoma of the breast were immediate and dramatic. The results in the pre-Halsted era were unbelievably bad. For example, von Winiwarter, who published a comprehensive study of Billroth's end results in 1878, reported 82 per cent of local recurrences and only 4.7 per cent of three year clinical cures. In 1898 Halsted reported his three year results in 76 cases. His local recurrence rate was 10 per cent, and his clinical cure rate 41 per cent. Willy Meyer had done his operation on a total of 44 patients by 1901. His three year clinical cure rate was 25 per cent. In interpreting these results we must remember that there was very little selection of cases for operation in these early days of the radical mastectomy. Almost all patients who came with carcinoma were operated upon. In Halsted's 1907 series, for instance, 76.4 per cent of his patients had axillary metastases.

The Mental Preparation of the Patient for Operation

Great care is devoted to the physiological preparation of patients with breast disease for operation, which is of course important for the patient's physical welfare. But little or no attention is usually given to the mental preparation of the patient for the surgery that she is about to undergo.

The main reason why the mental preparation of patients for breast surgery is so much neglected is that it can be done only by one person—the senior surgeon in whom the patient places her trust. The physical preparation of the patient can be, and usually is, a cooperative enterprise achieved by several bright young men whom the patient need not know personally. But the detailed explanation of what is to be done at operation, and why, and the inspiring of hope and the quieting of anxiety, must come from the individual whom the patient regards as *her* surgeon. It makes no difference whether she is a ward or a private patient. The responsible attending surgeon who has the patient's confidence should sit down with her, after he has examined her, and explain her problem to her as simply and as truthfully as possible. This takes time, and many surgeons today work at such a frantic pace that they have very little time to spend preparing their patients mentally for the operations they perform on them.

As I have already emphasized in Chapter 4 fear is the most important factor that deters women with breast disease from seeking medical help It has two aspects The first is fear of mutilation The modern woman reads a great deal about cancer and hears a good deal about it from her friends Her first thought when she discovers something wrong with her breast is that she has breast cancer She assumes the worst—that she will lose her breast It should be apparent to every physician who has had much experience with breast disease that the breasts—both breasts—are vitally important organs to every woman no matter what her age or marital status may be This fear of breast amputation often strikes so deeply that the woman cannot bring herself to consult a physician for a long time

A second and almost as important kind of fear that terrorizes women with breast disease is that they will not be cured of the cancer that they suspect they have. They have all known friends who were not cured and many have had relatives who succumbed We must not overlook the fact that laymen do not have much confidence in our ability to cure cancer

Many patients with breast disease get very little specific help from their surgeon to relieve these two basic fears—fear of mutilation and fear of death Their fears are either brushed off with a hasty reassurance or what is worse the surgeon attempts to calm the patient by lying to her A common practice is to tell the patient that her breast is to be removed because her tumor *may become* malignant Neither method is likely to succeed Most patients have enough intelligence to see through this kind of subterfuge They are then apt to lose confidence in their surgeon just at the time when they most need to rely upon him

In my experience the best weapon against these fears of breast disease is truth The truth must of course be told patiently and sympathetically It is important to emphasize its hopeful aspects But the word cancer should be used openly and frankly It has been my own practice to take as much time as is needed after I have completed my examination of the patient to explain to her in simple terms the diagnostic problem and how we propose to solve it, and what the possibilities in store for her are If the patient in question has a lesion that is probably benign I tell her so I *always* add that my clinical diagnosis is only a guess, and explain that the microscope is the final arbiter and that she may in fact have cancer Plans must be made for any eventuality When the lesion appears to me to be a carcinoma I tell the patient that there is a strong possibility that she has a cancer I point out however that my clinical diagnosis may be incorrect. I emphasize the fact that the hope of cure is excellent in early breast cancer If carcinoma is found at operation I tell the patient so without hesitation

When these truths are presented sympathetically to patients it has been my experience that they almost always rise to the occasion and accept them with courage and dignity Their fears are to some degree overcome by facing them I believe that I usually succeed in gaining the confidence of my patients and in persuading them that they can trust and rely upon me To some extent, no doubt, they transfer their burden to me.

Recently the problem of explaining the rationale of treatment for breast carcinoma to our patients has become much more complex because of our biopsy methods for sorting out those patients whose carcinomas have extended beyond

the reach of surgery, and who therefore should be treated by irradiation rather than radical mastectomy In preparing our patients mentally for what lies ahead of them, we must, therefore, tell them that even if cancer is found, the breast is not, under certain circumstances, removed Instead, treatment with irradiation is given

Another important advantage of telling the truth to patients with breast disease is that it makes them face the fact that they may have cancer, and that they must not delay treatment Patients who are not made to realize this possibility are apt to delay coming into the hospital, or to go shopping around from one surgeon to another while precious weeks and months slip by, and metastasis perhaps occurs

Personal Technique for the Halsted Radical Mastectomy

In my own surgical attack on carcinoma of the breast I have followed the fundamental principle that the disease, even in its early stage, is such a formidable enemy that it is my duty to carry out as radical an operation as the regional anatomy permits, without unreasonable penalty in function and appearance Just what this implies I will attempt to describe in the following pages The operation that I perform is essentially the Halsted radical mastectomy, but some of the details are derived from the technique of the late Dr George H Semken His carefully planned and meticulous methods of surgical attack upon several forms of cancer were my inspiration for special emphasis on this form of surgery I am indebted to Dr Allen O Whipple for my apprenticeship in silk technique, which adds, I believe, to the delicacy and exactitude of radical mastectomy It was under Dr Whipple's sympathetic direction that I was permitted to work out the technique for radical mastectomy here presented

The Anesthesia. If radical mastectomy is to be performed safely, the surgeon must have the intelligent and sympathetic cooperation of his anesthetist This begins with the anesthetist's preoperative visit to the patient on the night before operation On this occasion the anesthetist not only gets acquainted with the patient and gains her confidence, but he gets an impression of her cardiorespiratory reserve He evaluates the architecture of her airway and examines her teeth He inquires into drug idiosyncrasy He makes sure that her blood has been grouped and matched He advises extra fluids and sugar during the evening preceding operation

The anesthetist's premedication includes a barbiturate to insure a good night's sleep Morphine, 6 to 10 mg , and scopolamine, 0 3 or 0 4 mg , is given intramuscularly one and a half hours before the patient is brought to the operating room

For the type of radical mastectomy which I perform, we need a method of anesthesia which will maintain the patient at a relatively superficial plane of anesthesia over a period of between five and six hours Muscle relaxation is not required I do not mind, in fact, if the patient stirs slightly now and then Prolonged deep anesthesia is unnecessary and is chocking and hazardous

Our patients are usually induced with intravenous Pentothal Sodium Anesthesia is maintained with nitrous oxide supplemented with Pentothal Sodium, or Demerol, or morphine If Pentothal Sodium is used the amount given should be

kept judiciously small In our average patient with an anesthesia lasting between five and six hours the total dose of Pentothal Sodium is usually between 0 75 and 1 gram In patients with chronic cough resulting from sinusitis or the irritation of heavy cigarette smoking it is often desirable to use Demerol or morphine more freely as a supplement Our anesthetists do not use this type of anesthesia in patients with respiratory allergies ether being preferable in these cases

During the first stage of the operation when the skin flaps are being dissected and the electrocautery is being used explosive anesthetic agents cannot be employed but as soon as the cautery is disconnected it is possible to use ethylene cyclopropane, or ether Cyclopropane is the preferred anesthetic for patients with extreme hypertension and in certain other special types of cases

Our anesthetists observe certain special precautions in these long operations They take care to make the patient comfortable on the operating table They remove the mask from the face every hour to make sure that the skin of the face is not damaged They do not use airways unless they are absolutely necessary Finally they do not give too much fluid intravenously Unless my patients have a bleeding dyscrasia of some sort very little blood is lost in the operation as I perform it Although we have not attempted to measure the amount of blood lost in radical mastectomy I cannot believe that I lose anywhere near the average of 821 cc. that Coller and his associates reported

The average duration of the four radical mastectomies in which Coller measured the blood loss was 179 minutes It has been my observation that the more rapidly the operation is done the more blood is lost, and the more often transfusion is required. We take care not to give a total of more than 1500 cc of fluid intravenously Blood transfusion is rarely required If the blood pressure drops temporarily a blood substitute such as dextran usually brings it up again

The Position of the Patient upon the Operating Table There are certain details regarding the position of the patient upon the operating table (Fig 353) which are worth mentioning Both of the patient s arms are stretched out at right angles upon solid metal arm boards which will not give way and permit the arm to fall backward The brachial plexus can be injured in an unconscious patient if the arm is forced backward unreasonably The strap over the patient s legs, fastening her to the table should not be tight. The operating table should be one which can be tilted horizontally Side braces padded with small pillows are placed on the side of the table opposite to the diseased breast, so that when the table is tilted, the patient will not slide off It is desirable to incline the upper half of the operating table upward slightly so that the breast and the plane of the chest which form the operative field are horizontal

The skin of the arm on the tumor side is, of course prepared down to the elbow and the whole arm enclosed in a sterile stocking so that its position can be changed without breaking the sterility The chest wall is prepared from the neck to the umbilicus I do not use hexachlophene soap for skin preparation because it seems unreasonable to me to massage a breast which may contain cancer Iodine is undesirable for skin preparation because, unless great care is taken with it, it may pool beneath the patient s back and burn the skin I have compromised by using Zephiran for skin preparation.

For the first stage of the operation that is the dissection of the lateral skin

flap, it is helpful to have the operating table tilted away from the operator about 30 degrees so that the side of the breast and thorax are more accessible After this step has been completed, the table is turned back to a level plane

Operative Technique. The surgeon performing radical mastectomy aspires to carry out a complex maneuver so gently and precisely that every single cancer cell is removed from the operative field The operation should be done throughout with *sharp* dissection *Blunt* dissection should never be used Sharp dissection is done entirely with the knife The tissues are cleanly divided without being crushed Blunt dissection is done with scissors, with a hemostat, or with the surgeon's finger The tissues are scraped, torn, or pulled apart, and are badly mauled Emboli of cancer cells may be set free by blunt dissection

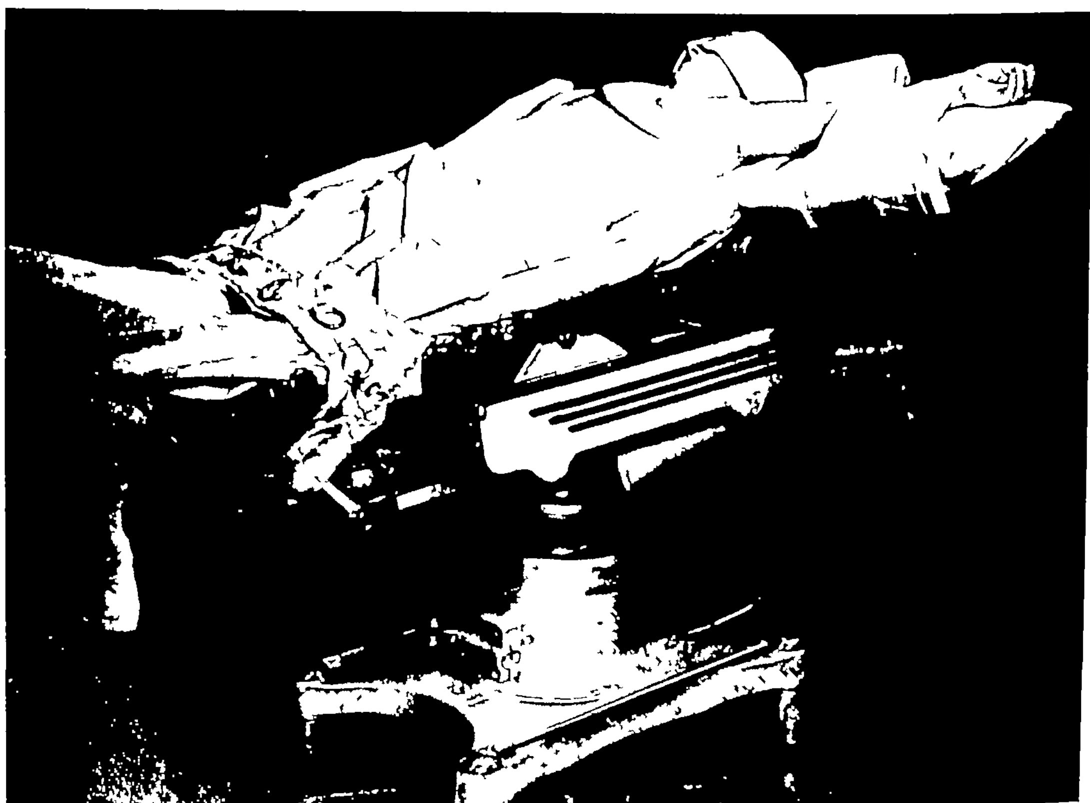


Fig 353 The position of the patient on the operating table The upper half of the table is slightly inclined upward and the table as a whole is tilted horizontally away from the operator so as to make the lateral aspect of the breast more accessible

I have found it preferable to use exclusively for hemostasis the smallest size curved clamp, sometimes called the mosquito clamp This clamp is similar to Halsted's original mosquito clamp except that the instrument he devised had a straight point and the one I prefer has a curved point It measures about 12 cm in length

I tie with No 5 black silk and use the same material for skin suture As compared with catgut, silk is so much finer and so much more pliable that the surgeon using it develops a sense of precision and delicacy which enables him to tie small vessels more accurately

The electrocautery is used for hemostasis only on the specimen, that is, on tissue which is to be removed

A special effort is made to keep the operative field covered with warm, moist

compresses or small towels leaving only the small area exposed in which dissection is actually being performed This prevents the tissues from drying out and minimizes shock and aids wound healing It is not possible to indicate in the accompanying drawings illustrating the steps of the operation the extent to which I keep the operative field protected with these moist compresses or towels, but I hope the reader will understand that it is my constant care

Since cancer cells are easily transplanted the surgeon must take care not to implant them The fact that viable cancer cells are present on instruments used for biopsy was proved long ago by Saphir As I indicated in describing my biopsy technique in Chapter 5 I take special precautions to avoid contamination of my mastectomy operative field by cells from the biopsy wound It is sealed with a rubber patch the only method that I know of which will surely keep serum and blood from escaping from it during the subsequent operative manipulations Gowns, gloves, drapes, and all the instruments on the tray used for biopsy are discarded before mastectomy is commenced I suspect that a leaking biopsy wound was the source of the carcinoma cells which Brandes and White transplanted from the breast to the donor site for a skin graft on the thigh If a surgeon *dissects* into carcinoma anywhere during the course of radical mastectomy he will inevitably implant it in other parts of his wound and fail to cure his patient This course of events is often obvious in the patients of surgeons who perform radical mastectomy upon patients with advanced and inoperable carcinoma

Step 1 The Dissection of the Skin Flaps The skin incision is outlined with methylene blue The *form* of the skin incision does not vary It consists of an oval or circle drawn around the breast with the tumor near its center Vertical extensions are then added above and below the circle The upper vertical extension is carried straight up to the strap line at the middle of the shoulder This vertical incision must be carried high enough up so that the axillary skin flap can be retracted sufficiently laterally to give adequate access to the axilla. The lower vertical extension is carried straight downward over the hypochondrium. This skin incision (Fig 354) is the one which Halsted finally came to use

In the standard American radical mastectomy the skin incision is carried out onto the arm over the anterior aspect of the pectoral fold as in the Willy Meyer operation This makes the dissection of the axillary flap a little easier but this axillary incision is by no means necessary When the upper incision is carried vertically sufficiently high in the strap line, perfectly adequate exposure of the axilla can be obtained with careful retraction. This vertical scar is hidden behind the shoulder strap and the patient can wear a sleeveless dress It should be emphasized that the worst mistake a surgeon can make from the point of view of good arm function is to carry the skin incision into the hollow of the axilla A vertical band of scar tissue bow stringing across the axilla is the inevitable result and arm motion is restricted Willy Meyer's original incision extended into the hollow of the axilla but he soon realized its disadvantage and placed it more cephalad so that it ran over the anterior aspect of the arm

A large number of different skin incisions have been devised. The more complex they are, the more they are to be avoided A transverse incision must be regarded in a special category of undesirability by itself It cannot possibly give

adequate access to the longitudinal extent of the operative field on the chest wall and the axilla

All types of skin incision which involve the cutting of flaps to cover the defect on the chest wall that remains when a wide removal of skin is carried out, are impractical because they do not do away with the necessity of skin grafting the donor area and they further prolong an already lengthy operation

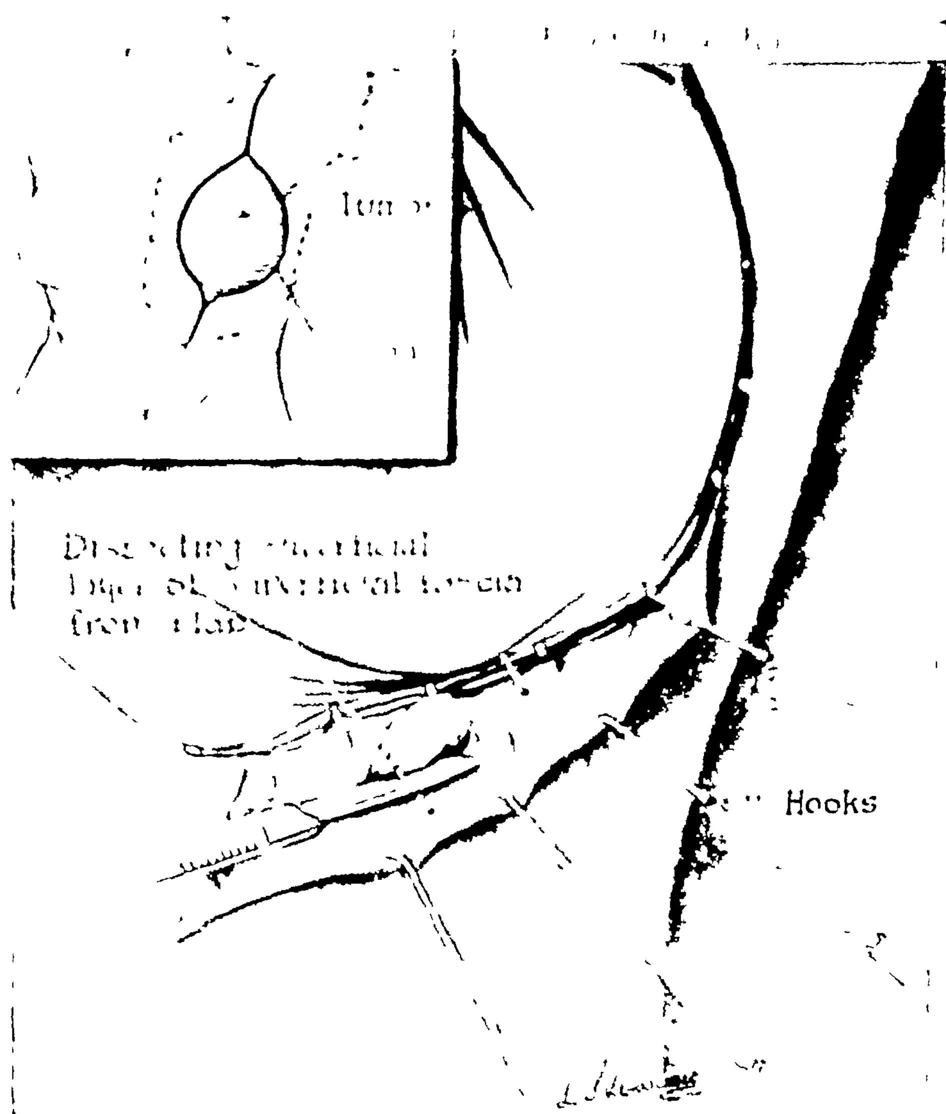


Fig 354 The skin incision for a carcinoma located near the center of the breast The dotted line shows the limits of the dissection of the flaps The dissection of the lateral flap begins at its lower end

Although I do not vary the simple basic form of my incision as a circle with upper and lower vertical extensions, I vary its position a good deal, depending upon the situation of the tumor in the breast If the tumor is situated medially or laterally, or cephalad or caudad, the circle is correspondingly shifted so that the tumor is in its center

The *extent* of the skin sacrificed depends not only upon the size of the tumor but upon the size of the breast As a general rule I include the skin over the whole of the protuberant breast When a tumor is eccentrically situated, an additional

area of skin is necessarily included When the tumor lies in the upper outer sector of the breast for instance an additional area of skin over the anterior axillary fold is sacrificed I try to place the line of skin incision at least four finger breadths, that is about 7 cm beyond the edge of the palpable tumor When the tumor is situated very high in the upper outer sector of the breast this is sometimes difficult to do Enough of a skin flap to cover the axillary vessels must be retained I have not seen skin recurrences in this region when this necessary compromise has been made I see no necessity for a muscle pedicle flap utilizing the latissimus to cover the axillary structures in these cases, as advocated by Moore and Harkins Other situations of the tumor in the breast do not limit the extent of the skin removal Thus, for tumors of the inner sector of the breast the area of skin removed regularly extends to the midline

The extent of skin removal is not planned with any reference to the closing of the wound with the exception that I have pointed out above for tumors high in the upper outer sector of the breast Knowing that a defect of any size can be easily covered with a skin graft I never hesitate to sacrifice as much skin as I think desirable from the viewpoint of curing the carcinoma The result has been that in almost every patient a defect of varying size remains when the skin flaps are finally approximated Since I know at the outset that I am going to have to do a skin graft, I never attempt to limit the amount of skin sacrificed I will return to this question of the amount of skin sacrificed when I discuss the frequency of local recurrence later on in the present chapter

I begin by dissecting back the lateral skin flap The first step is to make the skin incision Care is taken to carry the skin incision only down to the level of the superficial fascia (Fig 355) The knife must not plunge through this fascia into the subcutaneous fat. This delicate but distinct fascia is encountered just beneath the dermis Over the lower part of the chest wall it is thicker than over the upper chest wall but with careful hemostasis it can be identified all the way up the clavicle. Superficial to this fascia there is only a thin film of adipose tissue measuring not more than a millimeter or two in thickness and the skin itself Beneath this fascia lies breast tissue interspersed with a variable amount of fat. Close beneath the fascia lie relatively large thin walled veins, which might be called the *subfascial* veins of the breast. They are accompanied by small arteries and by lymphatics

It is a great convenience, from the viewpoint of good hemostasis, to keep the plane of dissection superficial to this fascia In so doing the troublesome subfascial vessels, which bleed freely are not cut, and the flap often can be dissected up without having to place a single hemostat on the flap itself Good hemostasis makes the dissection more precise as well as less shocking

Maintaining this level of dissection of the flap is even more important from the viewpoint of good cancer surgery In attacking carcinoma of the breast the surgeon must remove at least all of the mammary gland. We know from our pathological studies that carcinoma often extends widely throughout the breast tissue, and that not infrequently it is found as new and separate foci in areas of the breast remote from the dominant tumor Mammary tissue extends far more widely over the chest wall than the protuberant breast itself It may be found extending as a thin layer beneath the fascia which we have described, to the

midline of the sternum medially, to the edge of the latissimus dorsi muscle laterally, and above to the clavicle It often extends high into the axilla Hicken proved the wide anatomical extent of breast tissue nicely with injection studies The surgeon who intends to remove all the breast tissue must keep his plane of dissection superficial to the superficial layer of the superficial fascia, and carry it to these peripheral limits Unless this is done, mammary gland, as well as lymphatics accompanying the subdermal vessels, which are one of the routes along which breast carcinoma extends, will be left on the flaps

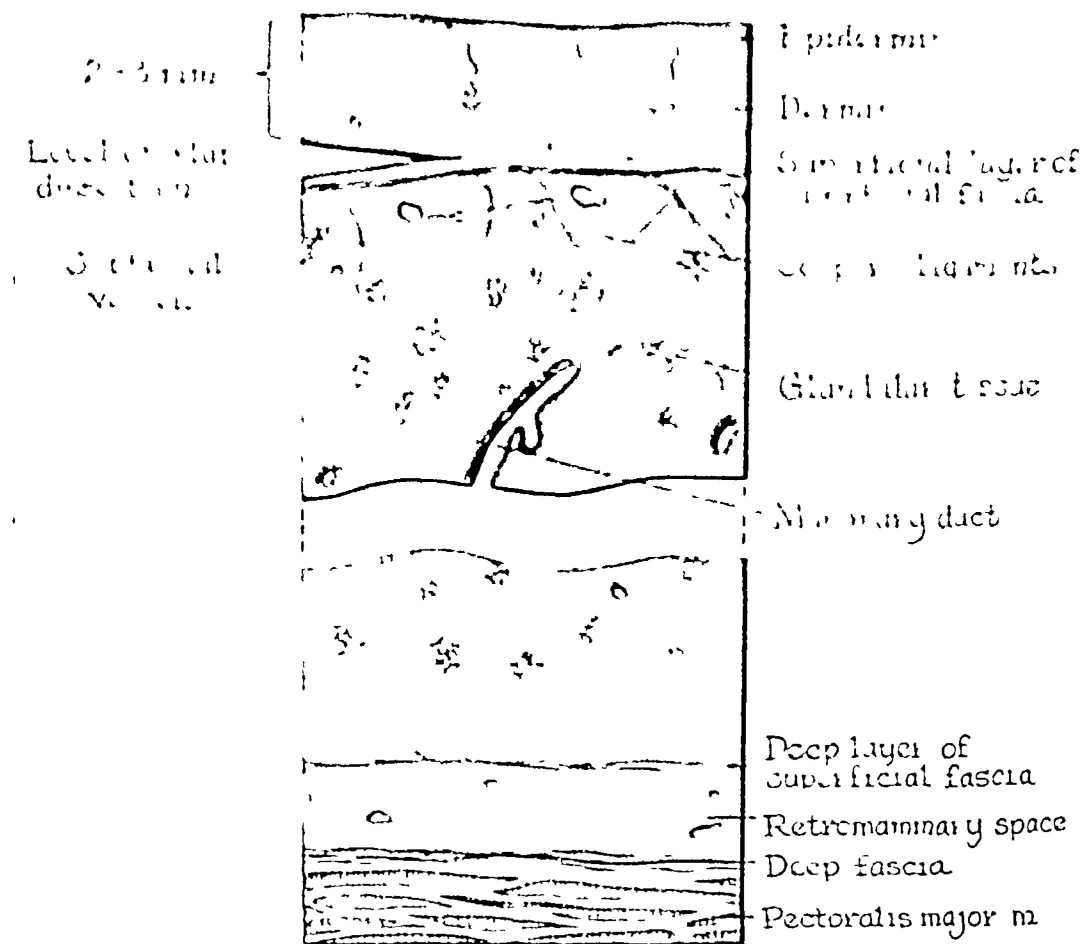


Fig 355 Diagrammatic cross section through the breast to show the level of dissection of the skin flap

It is convenient to begin the dissection of the lateral flap at its caudad end, and to work cephalad The flap is retracted laterally with light, sharp, single-pronged hooks (Fig 356) devised for this special purpose These hooks injure the flaps less than the various types of compressive forceps or toothed hooks usually employed In order to provide gentle countertraction from the breast side during the dissection of the flap, an ordinary surgeon's cap is clipped to the edge of the skin to be removed with the breast, using the larger size skin clips The first assistant then grasps his side of the cap and is thus able to provide countertraction for the surgeon dissecting up the skin flap, without having to press upon or paw the carcinoma-containing breast

As the caudad portion of the lateral flap is dissected away from the underlying

tissues the line of dissection finally reaches the latissimus dorsi muscle This marks the lateral limit of the elevation of the flap it is unnecessary to carry the dissection further posteriorly Semken liked to call the longitudinal fibers of the outer surface of the latissimus, as they were bared at the edge of the operative field, the *red line* He took care to develop such a red line down to muscle all around the edge of his operative field and used it as a definitive guide as to what was to be removed As the dissection of the lateral flap is carried cephalad the operator *must never lose sight of the latissimus* Particularly in obese patients, it is easy to lose sight of the muscle and to dissect either too far medially into the dangerous area of carcinoma-containing axillary tissues, or to dissect needlessly far posteriorly into the tissues over the dorsum of the posterior axillary fold.

At a point about halfway upward in the dissection of the lateral flap the skin hooks are changed to the cephalad half of the flap and its upper portion is dis sected up baring the pectoralis major muscle on the arm A bridge of tissue now

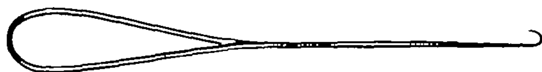


Fig. 356 Hook used for retraction in dissection of skin flaps.

remains across the axilla (Fig 357) with the naked fibers of the latissimus leading up to it from below and the naked fibers of the pectoralis leading down to it from above. The dissection of this axillary portion of the lateral skin flap is the final step in this phase of the operation It must be done meticulously for here axillary lymph nodes containing metastases may lie very close to the skin If the surgeon scrupulously keeps his plane of dissection superficial to the superficial layer of the superficial fascia in dissecting the axillary skin flap he will lay bare the apocrine glands of the axilla on the inner surface of his flap These are seen as small brownish nodules, interspersed with the roots of hairs They are an excellent guide to the operator in this region for unless they are exposed the flap is being cut too thick

At the base of the axillary portion of the lateral flap the red line along the latissimus becomes a white line as the tendinous portion of the muscle is laid bare Here several small intercostobrachial nerves and accompanying arteries and veins which cross over the white tendon at right angles to it, are encountered They must be isolated, clamped, cut, and tied with care otherwise the operative field is soiled with blood and good exposure of the axillary vein becomes more difficult. Finally the axillary vein is laid bare at a point where it crosses the white tendon of the latissimus (Fig 358)

The hemostasis along the whole length of the axillary flap is now carefully checked, and the flap is replaced against the chest wall so that it will not be angulated and its nutrition interfered with and is covered with a moist towel.

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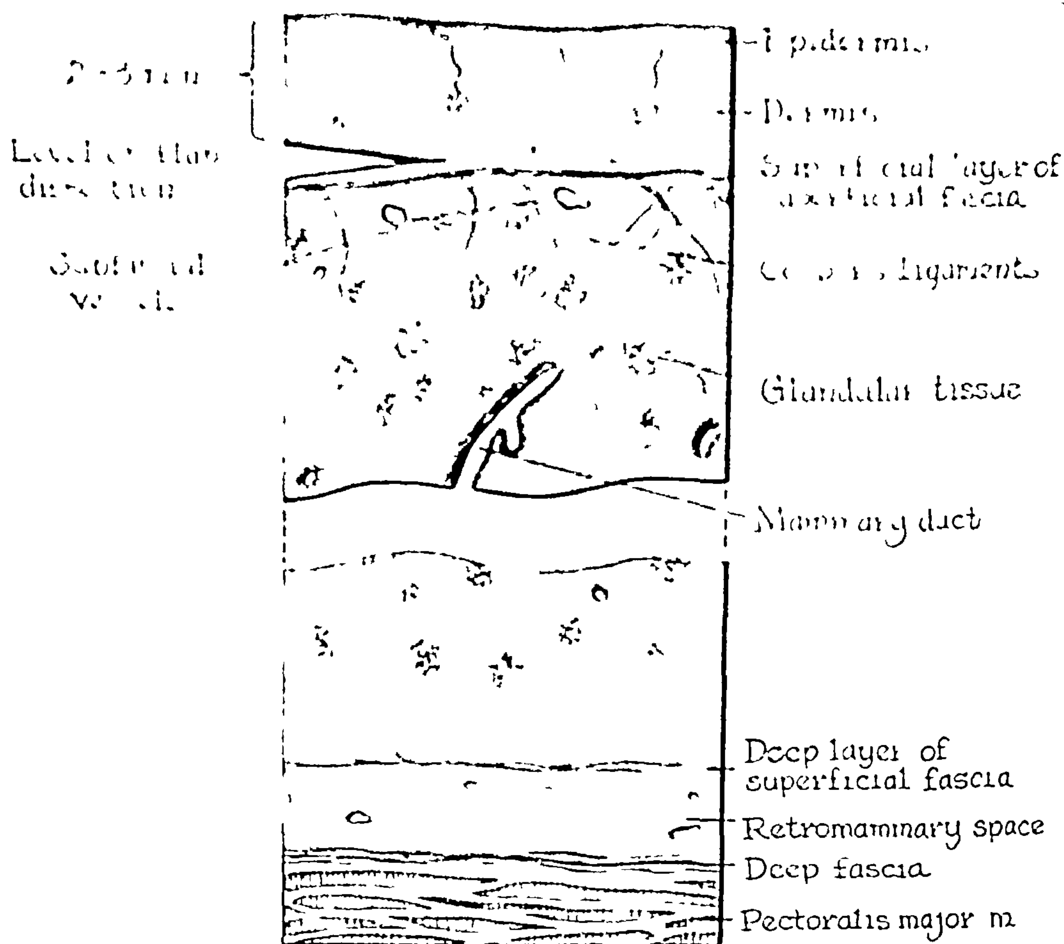


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As the caudad portion of the lateral flap is dissected away from the underlying

inner sector The red line at the base of the medial flap is carried upward along the midline of the sternum to the inner end of the clavicle The direction of the dissection then turns laterally and follows the lower edge of the clavicle In this area fibers of the platysma coming down from the neck are encountered and

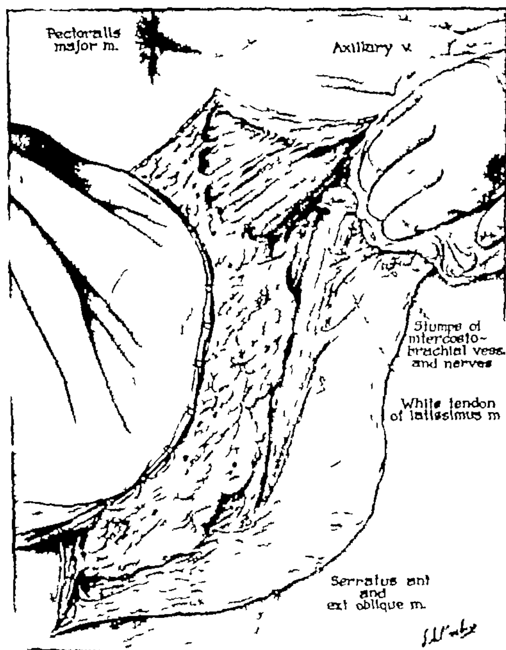


Fig 358 The dissection of the lateral flap completed, defining the axillary vein as it crosses the tendon of the latissimus.

severed When the dissection of this medial flap is completed a careful check of hemostasis is made, and the flap is laid back in place so that it will not be angulated, and covered with a moist towel

The skin flaps thus dissected up from the superficial layer of the superficial fascia and the breast tissue which lies beneath it, are thinner than the flaps that are cut in what might be called the standard American radical mastectomy My flaps are only 3 or 4 millimeters thick and consist of the skin covered with

The operating table is turned back to a level horizontal plane, preparatory to the dissection of the medial skin flap

The medial skin flap is then dissected back with the same technique used for the lateral flap (Fig 359) Again, it is convenient to begin at the caudad end of

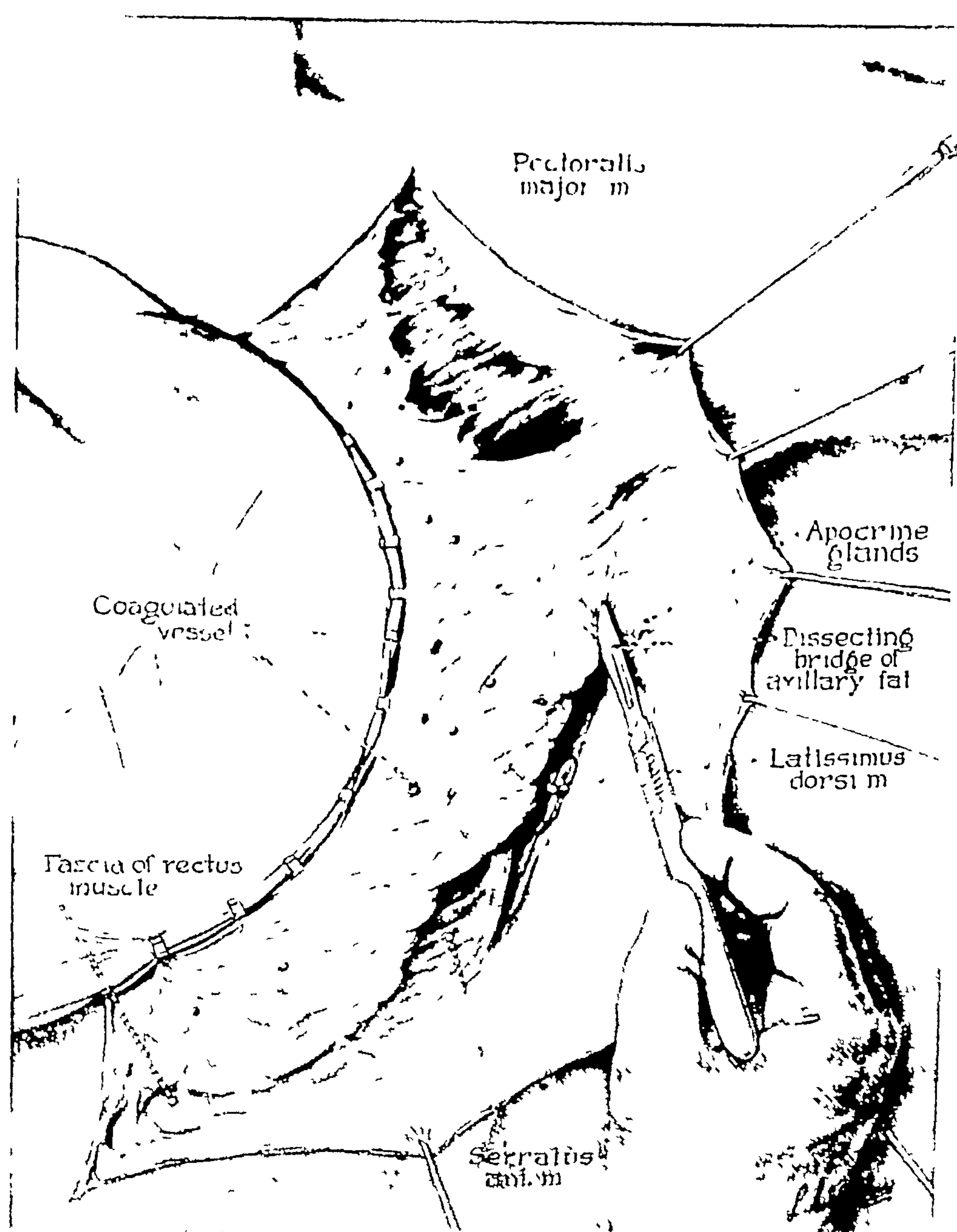


Fig 357 The upper and lower portions of the lateral flap dissected, leaving a bridge of tissue to be dissected from its axillary portion

the flap The dissection crosses medially over the rectus fascia to reach the midline of the sternum I do not remove the rectus fascia except in cases in which the carcinoma is situated in the lower inner sector of the breast Handley's pathological evidence of the permeation of this fascia with carcinoma was obtained from far advanced cases of the type which we would today classify as inoperable In cases which we have regarded as operable we have not seen permeation of the rectus fascia, but we nevertheless sacrifice it when the tumor lies in the lower

operator s technique, these thick flaps are shown The skin incision is carried directly down through the fat and mammary tissue to the muscle plane exposing the pectoralis major medially and the serratus muscle laterally Such thick flaps bear coarse lobules of fat and are several centimeters thick They are easily and quickly cut The dissection of thin flaps such as I have described is however a tedious procedure requiring about one and one half hours In my technique the pectoral and serratus muscles are not laid bare except where the red line crosses them at the periphery of the operative field These muscles remain covered with subcutaneous fat and mammary tissue after the flaps have been dissected The

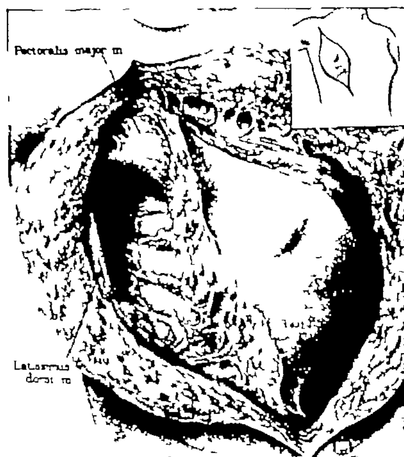


Fig. 360 The thick skin flaps of a widely used technique for radical mastectomy (From Harrington S W Carcinoma of the Breast. J.A.M.A. Vol. 92.)

difference in the extent and thickness of skin flaps in the standard American operation" and my operation is shown diagrammatically in Figs 361 and 362.

When the skin flaps are cut as thin as I have described the line of dissection must be exact, avoiding cuts into the corium, as well as too much tension Otherwise necrosis will occur It takes patience and a gentle hand to learn to cut these thin flaps and get perfect wound healing

I believe that the dissection of thin skin flaps all around the operative field is a logical development of Halsted s original operative plan and that the labor it entails is worth while The ultimate value of the method will of course, depend upon the demonstration of a decreased incidence of local recurrence

Step 2 The Dissection of the Pectoralis Major from the Arm The dissection at

only a delicate layer of fine fat lobules Halsted, in his original operation, dissected this kind of flap over the axilla, for he was a good gross pathologist and realized that a thick flap in this region implied dissection perilously close to the axillary nodes Elsewhere, however, his flaps were thicker, the incision being carried, in his own words, "through the fat." In defense of Halsted's technique

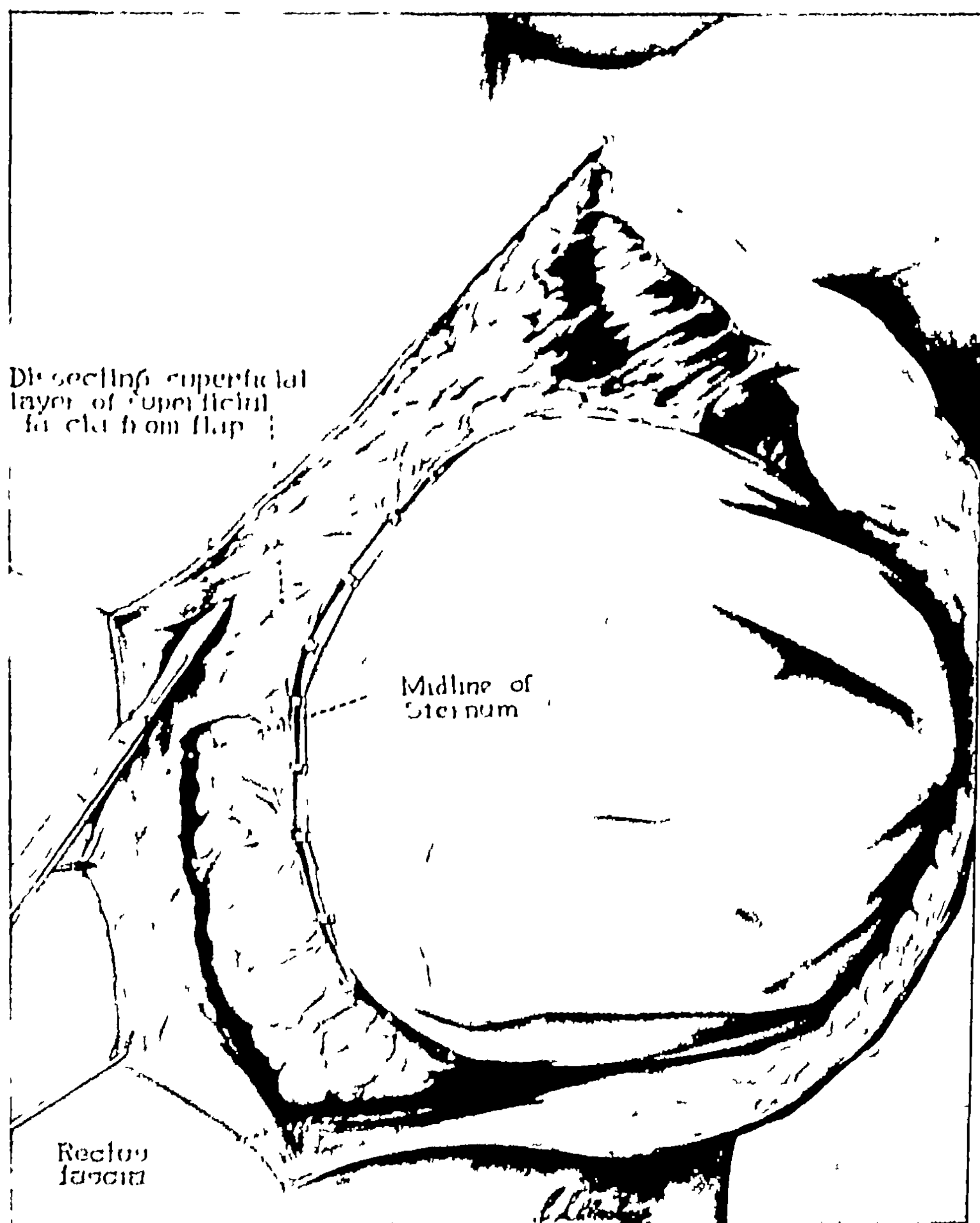


Fig 359 The dissection of the medial flap

it must be added that his excision was a very wide one, leaving such a large defect on the chest wall that skin grafting was regularly required

Most present day surgeons are much less radical Their skin excision is so limited that the edges of the flaps can be brought together and the wound closed Moreover, the usual practice is to cut thick flaps around the whole operative field, omitting even the dissection of the thin axillary flap that Halsted emphasized In Figure 360, reproduced from an illustration of a skilled contemporary

tages. The line of cleavage is a poor one and bleeding is annoying. Also when the clavicular portion of the muscle is left in place access to the apex of the axilla is not as good

Several atypical muscles may be encountered in the pectoral region The one most frequently found and most likely to confuse the operator is the so-called axillary pectoral muscle. Paul Eisler described and illustrated it very well As

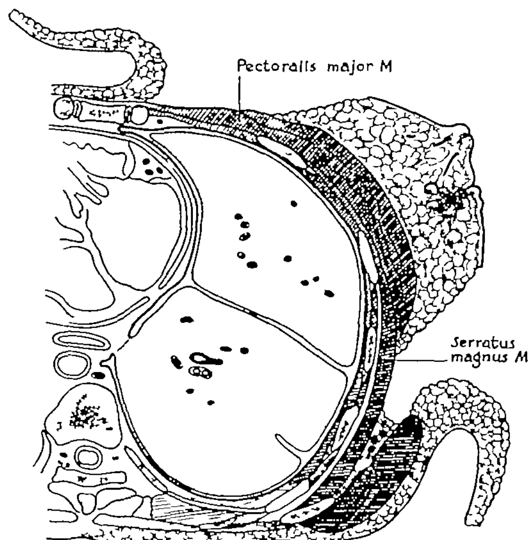


Fig 362. Diagrammatic cross section of breast through "Standard American" radical mastectomy A very limited area of skin over the breast is sacrificed. The skin flaps are long and thick, and as they are dissected the pectoralis muscle is bared medially and the serratus muscle is bared laterally

a short muscular band of varying thickness it arches from the white tendon of the latissimus dorsi up over the axillary vessels and nerves to join the tendon of the pectoralis major at its attachment to the humerus This muscle is well developed in the anthropoid apes and is present in about 7 7 per cent of human subjects of European stock In the dissection that I am describing, it must, of necessity be severed

Step 3 The Dissection of the Pectoralis Major from the Clavicle As the dissection of the pectoralis major away from the deltoid is carried medially along the

a deeper plane is begun by severing the attachment of the pectoralis major to the arm With the aid of lateral retraction at the base of the upper portion of the lateral skin flap, the surface of the pectoralis major is exposed The dissection is then carried laterally, clearing the muscle surface until the cephalic vein, separating the pectoralis from the deltoid, is identified and exposed The vein is followed out along the deltoid-pectoral groove until the apex of the pectoralis at its attachment to the humerus is reached (Fig 363) The muscle is then cut across at a

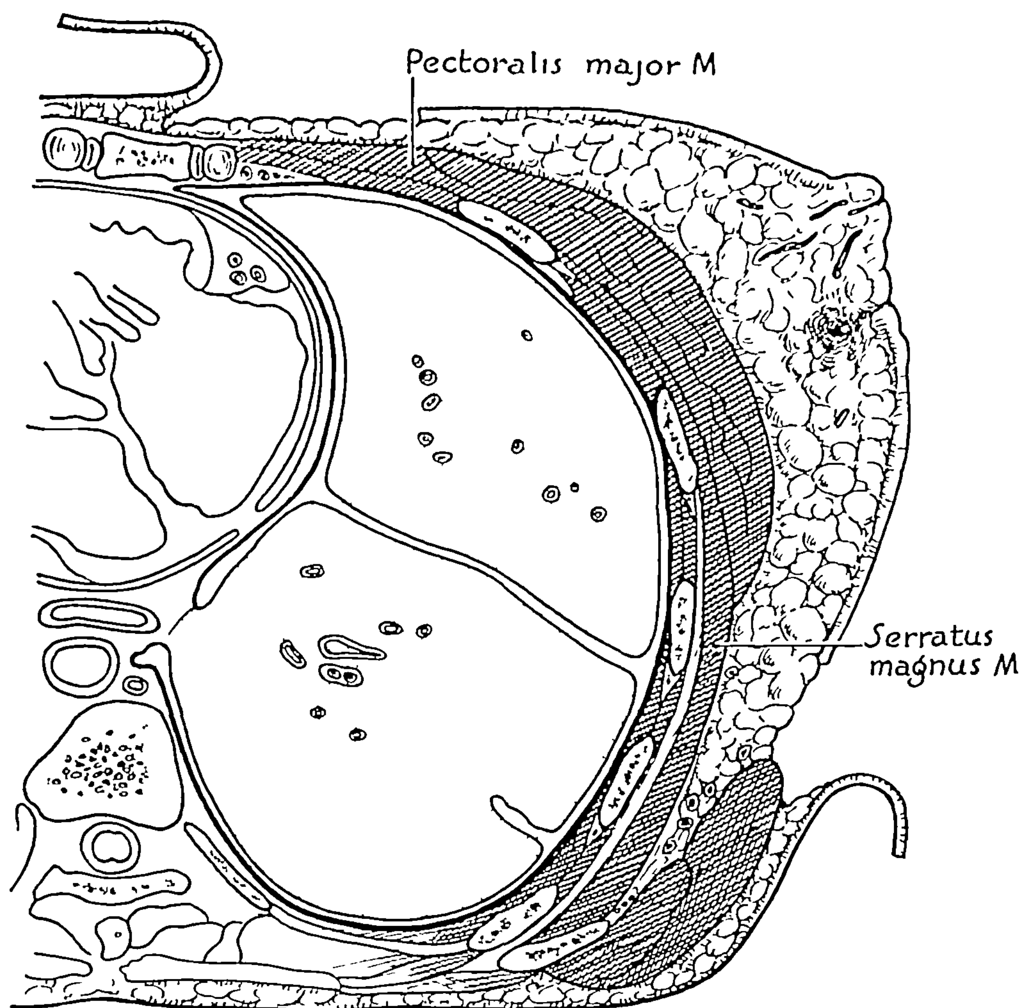


Fig 361 Diagrammatic cross section through radical mastectomy as I perform it A wide area of skin over the breast is sacrificed, and short thin skin flaps dissected back The pectoralis and the serratus muscles are not bared as the skin flaps are dissected

right angle to the direction of its fibers, 2 or 3 cm from its attachment to the bone The small muscle stump which remains contains two or three small vessels which should be carefully clamped and tied Most operators force a finger beneath the muscle and elevate it before severing it I do not find this necessary

After it has been detached from the humerus the pectoralis is dissected free from the deltoid along the cephalic vein and retracted caudad This dissection brings the deep pectoral fascia covering the deep structures of the axilla into view Many surgeons save the clavicular portion of the pectoralis, splitting the muscle between its pectoral and clavicular divisions This maneuver has two disadvan-

which are severed The first interspace is finally exposed as the muscle is cut away from its origin along the inner portion of the clavicle

Step 4 The Dissection of the Pectoralis Major from the Chest Wall The pectoralis major is now severed from its broad origin from the sternum the costal cartilages and ribs, and the fascia of the rectus and external oblique muscles allowing the whole operative specimen to fall laterally to the patient s side (Fig. 364) This can be the bloodiest and most shocking part of the operation unless it is done with good hemostasis.



Fig. 364 The dissection of the pectoralis major off the chest wall.

I begin this phase of the dissection by clearing the first interspace down to the intercostal muscle, at a point near the inner end of the clavicle The thick edge of the pectoralis major muscle is retracted caudad and elevated from the second rib using a small cheek retractor In this way a plane of cleavage is developed between this muscle and the thoracic cage. With the muscle thus elevated its detachment is begun from its origin from the inner end of the clavicle, the cartilage of the first rib the manubrium and the inner end of the first interspace Several branches of the first perforating artery and vein will be encountered as this portion of the muscle is severed. The trunks of the first perforating artery and vein usually come into view near the caudad edge of the inner end of the interspace, as they arch up over the second costal cartilage They should be care

cephalic vein to the apex of the triangle which the deltoid forms with the clavicle, the thoraco-acromial vessels come into view The pectoral branches of the thoraco-acromial artery, the accompanying veins, and the lateral anterior thoracic nerve emerge from the deep pectoral fascia just medial to the medial edge of the pectoralis minor, and stretch across the operative field to enter the deep surface of the pectoralis major They should be carefully isolated, clamped, cut, and tied To facilitate this part of the dissection the operator should retract the pectoral muscle caudad with his left hand

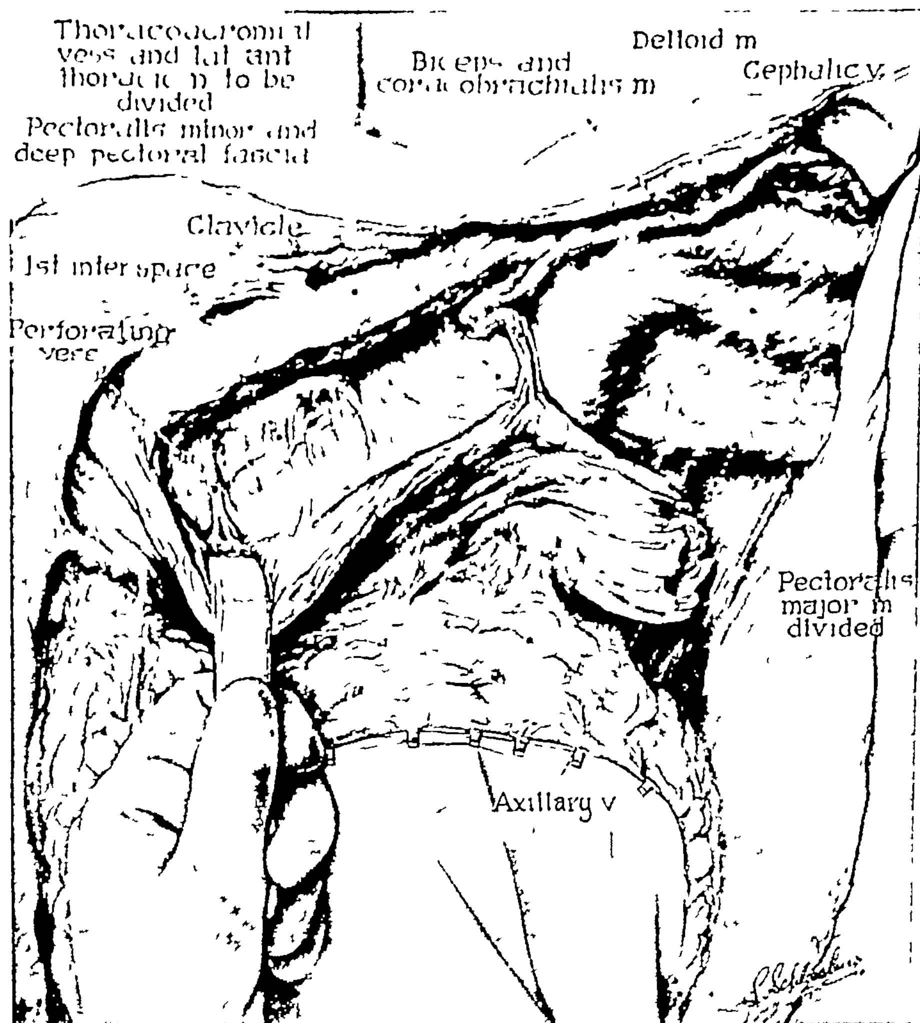


Fig 363 Severing the attachment of the pectoralis major to the humerus and to the clavicle

The deep pectoral fascia itself is not disturbed at this stage of the operation Beneath this strong fascia which encloses the pectoralis minor, lie the axillary vessels and nerves, and the lymphatics and lymph nodes, in which we are particularly interested All our dissection at this stage of the operation is carried out superficial to this fascia

The dissection is then carried medially, severing the attachment of the pectoralis major to the clavicle by cutting across its fibers parallel to and about 1 cm below the lower edge of the clavicle Leaving a little of the muscle on the clavicle in this way makes it easier to clamp and tie the series of small vessels

tracted caudad and laterally giving access to its origin from the third, fourth and fifth ribs

The attachments of the muscle to these ribs are then severed proceeding from the third rib downward The muscle is friable and difficult to retract. The most convenient way to deal with it is to pick it up with thumb forceps Along the edge of each rib several tiny vessels will be severed as the muscle fibers are cut across The pectoralis minor interdigitates with the serratus anterior and it requires a little special attention and practice to learn to distinguish the pectoralis minor fibers from those of the serratus digitations which lie beneath them and which should not be cut

The pectoralis minor is allowed to fall laterally with the pectoralis major and overlying tissues already severed from the chest wall and the dissection is continued in that portion of the operative field just caudad to the origin of the pectoralis minor In this region the dissection of the specimen off the chest wall should include the careful removal of the fascia over the digitations of the serratus

This dissection of the serratus fascia is carried posteriorly the specimen being allowed to fall away to the patient s side, until the edge of the latissimus comes into view in the caudad part of the field It is then desirable to suspend the dissection of the specimen off from the chest wall because its detachment can be more conveniently completed after the axilla has been dissected.

Before going on to the next stage all clamped vessels on the thoracic wall should be tied, hemostasis checked and the whole area of denuded thorax carefully covered with moist compresses

Step 6 The Dissection of the Axilla The axilla now lies before the operator like an open book. When the arm lies beside the trunk, the axilla may be thought of as a cleft between the upper arm structures and the thoracic wall When the arm is abducted at right angles to the trunk, however as in radical mastectomy the cleft becomes a tetrahedral space, with its apex at the clavicle and its base at the pit of the axilla. The three elongated triangular walls of this space are then formed by the shoulder structures cephalad, the chest wall caudad, and the pectoral muscles ventrally In the Willy Meyer and standard American technique for radical mastectomy in which the axilla is dissected before the pectoral muscles and the breast are removed from the chest wall the surgeon s access to the axilla is not good because the structures forming its ventral wall (the axillary prolongation of the breast and the fat usually found in this region, and the pectoral muscles) constitute a bulky mass which tends to slide down into the field of dissection in the axilla. In the Halsted technique for radical mastectomy which I am describing, this bulky mass of tissues is out of the operator s way when he dissects the axilla, for with the dissection of the breast and pectoral muscles off the chest wall at an earlier stage in the operation they have fallen to the patient s side Any surgeon who has compared the ease of access to the axilla with these two different techniques will at once realize the advantage, from this point of view of the Halsted procedure Instead of having to dissect in the depths of a deep narrow cleft, handicapped by the need for constant retraction of the overlying tissues, the surgeon can work at ease in a comparatively flat field without

fully isolated, and clamped before they are cut A little more laterally, in this same interspace, a much smaller perforating vessel, the first of a series of minor perforators which emerge parallel to and at a point 3 or 4 cm lateral to the main perforating vessels, should be identified, and clamped before it is cut

The dissection is then carried caudad, severing the pectoralis major from its attachment to the sternum and the costal cartilages and ribs The perforating vessels at the sternal edge in the successive interspaces are identified as they come into view and clamped before they are cut The position of these vessels in the lower interspaces is variable, sometimes they emerge just below and sometimes just above a costal cartilage The intercostal spaces should be meticulously cleared of all fat and areolar tissue as the dissection proceeds As the thoracic cage is thus denuded it should be covered with warm moist compresses or a towel in order to prevent drying of the tissues and consequent shock The operative specimen is allowed to fall laterally and is similarly covered with a protecting towel

When the dissection of the pectoralis major from the chest wall has been carried laterally to a point where the fan-shaped edge of the origin of pectoralis minor comes into view, it should be discontinued This is a convenient point at which to pause and tie the many clamped vessels, getting rid of the mass of clamps that have accumulated as the chest wall has been cleared The pectoralis minor must now be dealt with in a separate step

Step 5 Severing the Attachments of the Pectoralis Minor In this step, the pectoralis minor muscle is cut across 2 or 3 cm from its insertion on the coracoid process, and is turned back from over the axillary structures and the chest wall very much as the pectoralis major was dissected back To free the pectoralis minor an incision is first made through the deep pectoral fascia along the lateral edge of the muscle, near its cephalad end, where it becomes tendinous The free edge of the muscle is then picked up with forceps and it is cut across. One or two vessels which are encountered in its substance are carefully clamped and tied I do not find it necessary or desirable to force a finger beneath the muscle, elevating it from the underlying axillary vein, as most operators are accustomed to do This maneuver is apt to cause hemorrhage which obliterates the anatomical details which the operator needs for a meticulous axillary dissection which shortly follows

A tiny branch of the thoraco-acromial artery, which usually enters the pectoralis minor along its medial edge just caudad to the point where it has been transected, should be identified and clamped and cut Although this vessel is tiny, it bleeds freely and obscures the operative field if it is torn off as the muscle is dissected back

The pectoralis minor is then gently retracted caudad, exposing its deep surface and baring the areolar tissue covering the axillary structures Since the axillary dissection is a separate and later step in the operation, I take care not to disturb these axillary structures at this stage The axilla is, so to speak, uncovered but not dissected The vessels and nerves which emerge from the areolar tissue of the axilla and stretch across it to enter the deep aspect of the pectoralis minor are clamped and cut close to the muscle This frees the muscle so that it can be re-

custom of some operators if the nodes contain metastases this is a splendid way to implant carcinoma cells throughout the operative field and to insure local recurrence Another disadvantage of the scraping or pawing technique in the axilla is that small vessels are torn They bleed and the fine details of the anatomy are obscured It becomes impossible to do a meticulous dissection Every vessel, even the most minute, must be identified and clamped before it is cut if the requisite perfect hemostasis is to be achieved Only with this kind of technique can all of the many small lymph nodes be seen and included in the tissues removed I use smooth rather than toothed forceps in my dissection because I fear that toothed instruments may pierce carcinomatous nodes and pick up and reimplant carcinoma cells I try indeed to avoid grasping nodes even with smooth forceps Very little traction is needed and usually it can be exerted through clamps on the specimen side of the vessels that are divided Hooked retractors should never be used in any cancer operation

The deep pectoral fascia having been incised over the brachial plexus the fascia thus released and the fat and areolar tissue attached to it are dissected caudad, bringing the wall of the vein into view Its ventral and caudad surfaces are meticulously cleared from the level of the thoraco-acromial vessels laterally to the point where the vein crosses the white tendon of the latissimus The branches of the vein are isolated as they are encountered, and are clamped before they are cut. They vary greatly in number and arrangement. Only one thing need be kept in mind they should all be sacrificed The axillary vein occasionally divides into two main trunks These of course should both be preserved I have not found it necessary to sacrifice the axillary vein on account of the extent of the axillary metastases If our criteria of operability are followed cases in which nodes containing metastases are adherent to the vein and those in which the wall of the vein is involved, will not be operated upon It may well be that the axillary vein can be excised without much penalty as Neuhof Faugère, Lobb and Harkins and Macdonald have maintained, but I see no excuse for the procedure I am convinced that all cases in which the vein is involved are incurable

It is not necessary to remove the fat and areolar tissue overlying the brachial plexus. Lymph nodes are not found lying cephalad to the axillary vein except in the vicinity of the thoraco-acromial vessels We have occasionally found one or two nodes in this region and it is therefore our custom to clear the stumps of these vessels with care

A small detail concerning the dissection of the axillary vein is worth mentioning. At a point from 1 to 3 cm lateral to the origin of the thoraco-acromial vessels the axillary vein is usually crossed obliquely by a small artery and nerve (Fig 366) The artery enters the deep surface of the pectoralis minor and sometimes sends a branch onto the adjacent chest wall. Its origin is hidden above and behind the vein where the surgeon does not see it, but it is from a common trunk with the thoraco-acromial axis in about one half of the anatomical subjects I have studied and as a separate branch from the main artery 1 or 2 cm lateral to the thoraco-acromial trunk in the other half of the subjects It is not described in the anatomical texts which I have consulted so that I have had to designate it simply as the *artery to the pectoralis minor* The nerve which accompanies this small artery is the medial anterior thoracic nerve, which also supplies the pec

any retraction except that provided by the weight of the specimen itself as it falls to the patient's side

The objection usually voiced against the technique of excising the breast and pectoral muscles from the chest wall before attacking the axilla is that it increases the chance of distant metastasis I do not believe that this is a fact The axillary route for metastasis, of course, remains open during the period required to dissect the breast and pectoral muscles from the chest wall, but we do this without any handling of the breast itself and with only the gentlest kind of retraction on the muscles close to the point at which they are cut from the chest wall It should be emphasized, on the other hand, that in the final stage of the "standard American

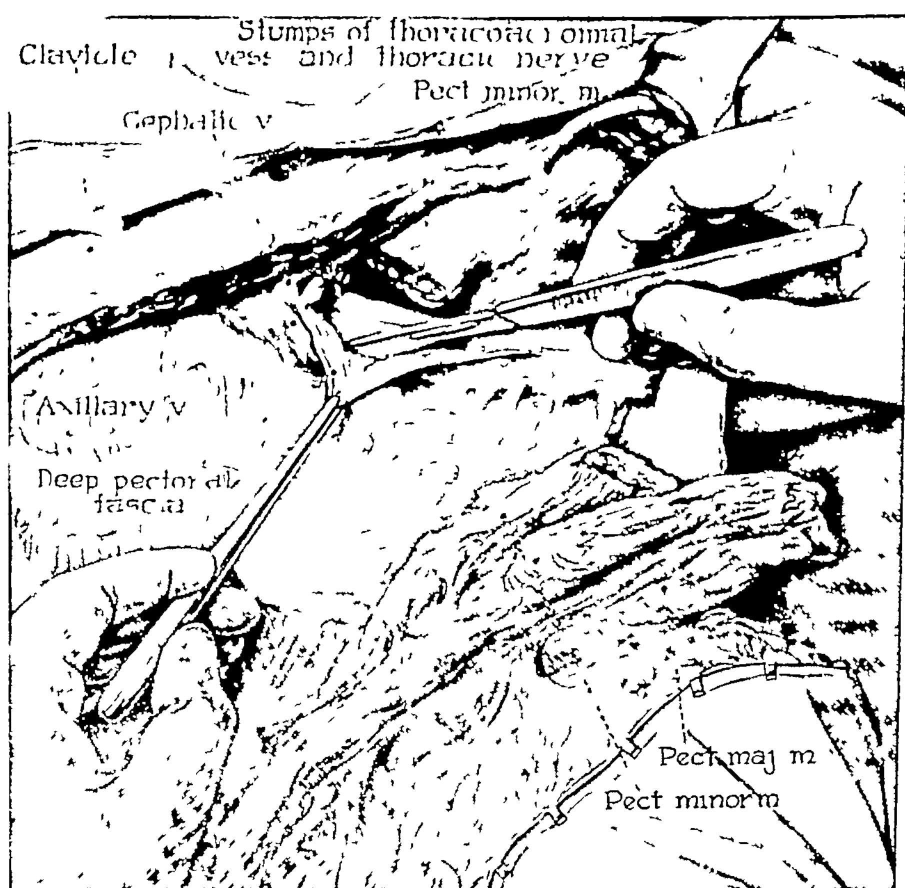


Fig 365 Beginning the dissection of the axillary vein with smooth forceps and scalpel

radical mastectomy" in which the breast and the pectoral muscles are retracted medially as they are severed from the chest wall, strong traction on the specimen is required and a considerable degree of pressure is often exerted upon the tumor itself Even though this takes place after the lymphatic pathway through the axilla has been severed, I fear that it may squeeze tumor emboli into lymphatic trunks which still remain, particularly those to the internal mammary nodes

The dissection of the axilla is begun by incising the deep pectoral fascia over the brachial plexus, parallel to and slightly cephalad to the axillary vein The fascia is picked up with smooth forceps and incised with a sharp knife (Fig 365) All my axillary dissection is done with smooth forceps and the knife I never scrape the axillary contents out with a gauze sponge over the finger, as is the

tissues away from the thoracic wall already begun at the apex of the axilla The sheet of fascia over the digitations of the serratus is gently retracted laterally and dissected off this muscle The intercostohumeral nerves spanning the axilla transversely and the lateral cutaneous branches of the intercostal nerves and their accompanying vessels, are encountered and sacrificed as this dissection is carried dorsally In the depths of the cleft between the naked serratus digitations and the sheet of fascia retracted laterally the long thoracic nerve of Bell finally comes into view It lies in the fat just beneath the surface of the fascia which has been retracted laterally An incision is made through the fascia along the lateral edge of the nerve and it is allowed to drop back medially against the chest wall out of the way of subsequent dissection



Fig. 367 Dissection of fascial plane from the chest wall as part of the axillary dissection

I then return to the axillary vein and complete its dissection beginning at its medial end and working laterally The vein is lifted up with a small vein retractor and the *branches on its caudad aspect are clamped cut, and tied one by one as the dissection proceeds laterally The mass of tissue between the medial portion of* the vein and the chest wall is dissected downward and outward off the surface of the subscapular muscle leaving the long thoracic nerve as the only structure crossing the medial part of the axilla in a longitudinal direction This nerve must under no circumstances be cut If patients are properly selected for operation the nerve will not be found to be involved by disease and there is no reason for sacrificing it Cutting this nerve produces the ugly deformity of wing scapula " Patients in whom the nerve has been cut or damaged also complain of a good deal of shoulder pain for months afterward—why I do not know

When the dissection of the tissues from the subscapular muscle reaches a point where the thoracodorsal nerve is encountered as it arches down from beneath the axillary vein to join the thoracodorsal vessels, a decision has to be made whether to sacrifice or to preserve it.

This nerve during the last 8 or 10 cm of its course before it enters the latissimus muscle, lies among the lymph nodes of the central and scapular group It seems unreasonably hazardous to dissect the nerve out from among these lymph nodes if it is likely that they contain metastases I almost always sacrifice it I

toralis minor Both the artery and the nerve are closely applied to the ventral surface of the vein in their oblique course across it, and it is from this fact that their importance to the surgeon arises Since we strip the axillary vein clean we necessarily identify and sever these two structures which cross over it A small vein is usually found emptying into the axillary vein just beneath the crossing artery In isolating, clamping, and cutting the artery and nerve, care should be taken to identify and clamp this small venous branch before it is torn and the operative field soiled with blood

When the ventral and caudad aspects of the axillary vein lateral to the thoraco-acromial vessels have been cleared, I turn my attention to the apex of the axilla I dissect the fat and areolar tissue off the axillary vein medially to the point where

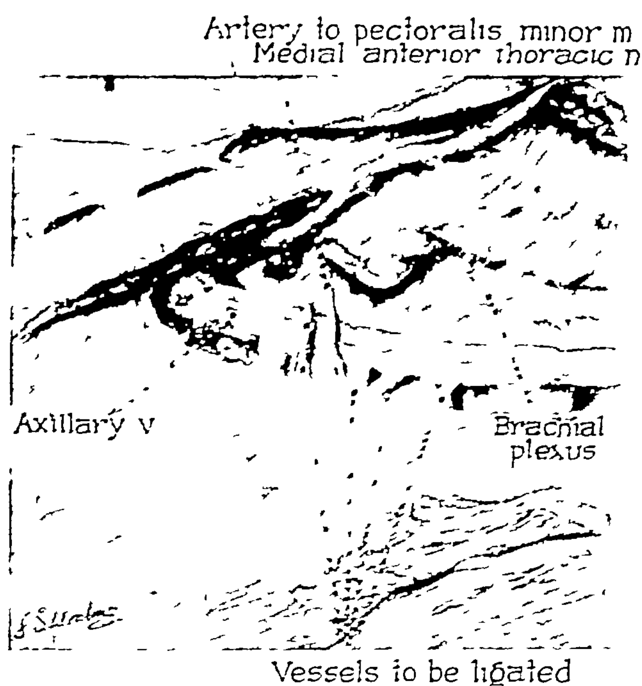


Fig 366 Artery to the pectoralis minor and the medial anterior thoracic nerve crossing the axillary vein

it crosses beneath the subclavius muscle The reflection of the deep pectoral fascia onto the chest wall opposite the upper portion of the vein is then dissected away from the chest wall to the apex of the axilla (Fig 367) The mass of fat and areolar tissue thus mobilized in the cleft between the chest wall and the most medial portion of the axillary vein contains the highest axillary lymph nodes and the lymphatic trunks that pass upward beneath the clavicle to empty into the confluence of the subclavian and internal jugular veins A clamp is placed across the apex of the mass as high as possible and it is cut across and ligated in order to avoid backflow of lymph into the wound and to secure the small blood vessels which are usually included within the clamped tissue A single long marking tie is placed around the apical tissue to orient the pathologist in his study of the specimen

The next step in the operation is to continue the dissection of the axillary

in order not to damage the nerve The fascia over the serratus at this deep level is therefore not disturbed

In this last phase of the operation a little outward traction on the specimen as it lies on the table at the patient s side enables the operator to roll so to speak the remaining tissues laterally over the latissimus dorsi In this process the branches of the thoracodorsal vessels which turn medially to supply the chest wall opposite the apex of the subscapular and teres major muscle body as well as those which enter the latissimus itself are isolated clamped and ligated These vessels are of considerable size and the region has been aptly called the bloody angle of radical mastectomy With the technique which I have described here however there is no need of any hemorrhage, for the surgeon s access is good and the vessels easily identified

It now remains only to cut the specimen free from the edge of the latissimus dorsi to complete the dissection The specimen falls of its own weight into the basin which a nurse holds at the side of the operating table to receive it. The dissection has been completed with a minimum of traction and handling of the specimen and a correspondingly lesser chance of the surgeon s disseminating the carcinoma. The operative field at the end of the specimen is shown in Figure 369

Step 7 The Closure of the Wound The whole extent of the wound is now carefully inspected to be sure that it is dry for if it is to be closed without drainage as is our custom hemostasis must be meticulous The surgeon must also always make sure that he has not left any sponges beneath the flaps

The skin flaps are then replaced on the chest wall and sutured together at the upper and lower ends of the wound with interrupted sutures of No 5 silk. The suturing is carried only as far as the flaps will come together without too much tension. By this I mean a degree of tension which will not cause necrosis My flaps are so thin that the amount of tension required to damage them is slight. The operator has to learn by experience what is safe Blanching of the skin of the flap beyond a suture is the best sign that too much tension has been used

I strongly advise against suturing the skin flaps down upon the chest wall as recently recommended by Larsen and by Keyes and his associates

A defect of varying size remains on the chest wall. This is rarely less than 15 cm. in diameter and may be considerably larger The edges of the skin flaps around the defect are sutured down to the fascia over the intercostal muscles and to the serrati muscles with interrupted sutures of silk, their ends being left about an inch long and laid out on the surface of the flaps, so that they can be easily picked up when it is time to remove them (Fig. 370)

The defect is covered with a split thickness, or Thiersch graft (Fig. 371), which is usually taken from high up on the postero-lateral surface of the right thigh I find that the Reese dermatome is a convenient instrument with which to take the graft I use the No 14 shim which gives a moderately thick graft. If this instrument is used the graft should be removed from the adhesive tape upon which it is held upon the drum The graft is then cut to fit the defect on the chest wall and sutured edge to edge with a running suture of Dermalon, on a swedged curved needle The graft should be perforated in several places over the inter spaces, so that if serum or blood accumulates beneath it, it may escape I take

have preserved it only in patients whose carcinoma was very small and well differentiated, without, of course, any clinical evidence of axillary metastases The paralysis of the latissimus which results, with slight weakness of adduction and internal rotation of the arm, is scarcely perceptible

If the thoracodorsal nerve is preserved it is drawn medially and dissected away from the thoracodorsal vessels

The thoracodorsal vessels themselves are always sacrificed in my technique They are clamped, cut, and tied just beyond the point where the scapular circumflex branches are given off

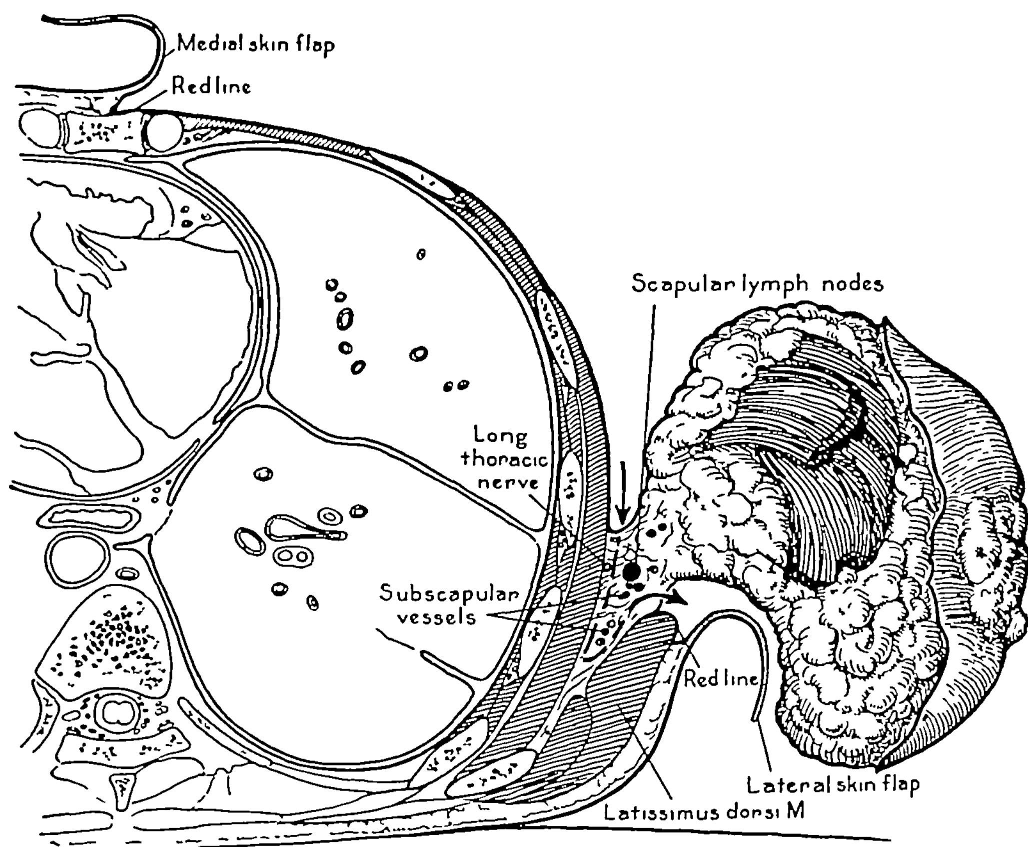


Fig 368 The final step in the dissection seen in cross section—the excision of the specimen from its attachment along the groove between the serrati and latissimus muscles

When the axillary vein has been cleared all the way out to the point where it crosses the outer edge of the white tendon of the latissimus dorsi muscle, and the thoracodorsal vessels and nerve severed, the mass of axillary tissues, now freed from all its medial and cephalad connections, is dissected in a caudad direction down over the surface of the pyramidal muscle body formed by the subscapularis medially, and the teres major and the latissimus dorsi laterally

The final step in the axillary dissection is the excision of the specimen from along the groove between the chest wall and the latissimus dorsi, its only remaining attachment This is carried out along a longitudinal plane, and from the chest wall toward the latissimus as shown by the arrows in Figure 368 When, in this final stage, the dissection reaches the level of the long thoracic nerve as it lies upon the serratus fascia, the operator must take care to dissect more superficially

Step 8 The Operative Dressing The application of the operative dressing is an important part of the operative technique and if good wound healing is to be achieved the dressing must not be left to an assistant who is unfamiliar with its details. The skin graft is covered with a single layer of Xeroform impregnated

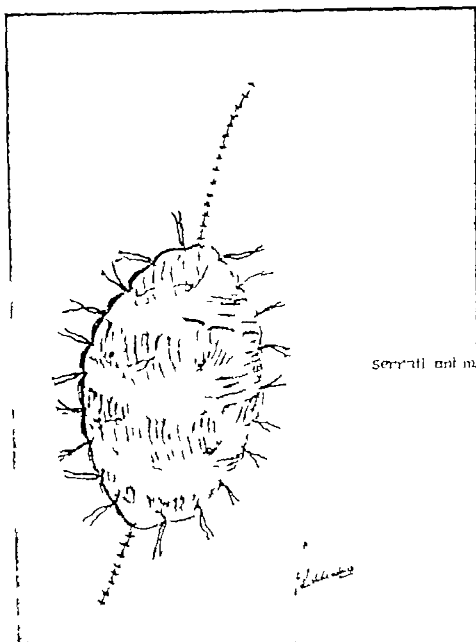


Fig. 370 The operative wound with the flaps sutured in position ready for grafting.

gauze (never Vaseline gauze) to keep the graft from sticking to the dressing I apply gentle pressure to obliterate the dead space in the axilla and to hold the graft in contact with the chest wall I use fluffed gauze to obtain this pressure and although I have tried other materials, I have found none which is its equal for this purpose The forearm is laid across the upper abdomen encased in a layer of absorbent cotton Two eight inch ace bandages are then applied, not too tightly

great care to be sure the bed for the graft is absolutely dry before applying it, but even with this precaution, there is occasionally some oozing beneath it which may balloon the graft up unless it is perforated

No drains are used If hemostasis is meticulous none is required In occasional patients an accumulation of blood or serum may develop beneath the lateral

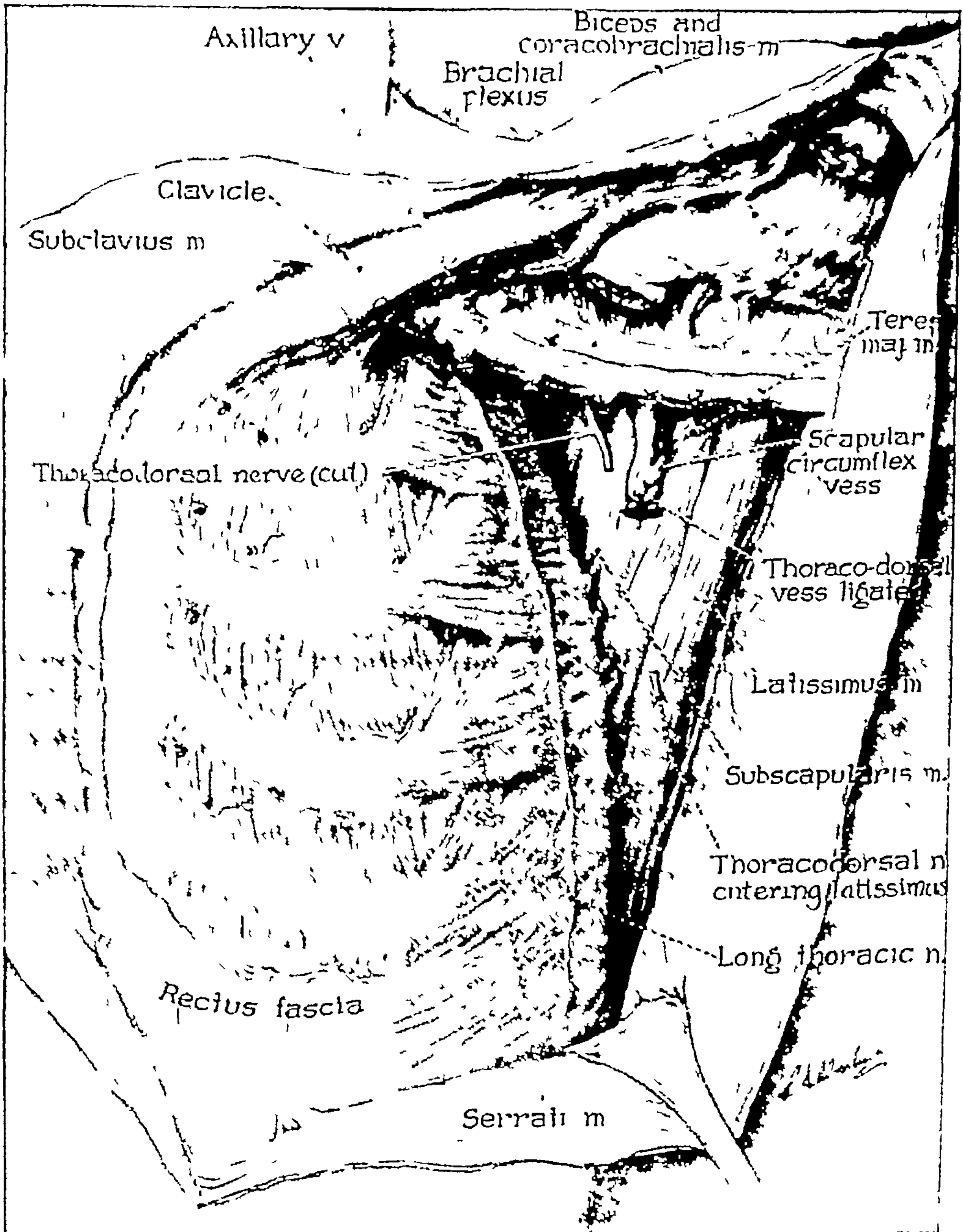


Fig 369 The operative field at the completion of the dissection

flap, but this is easily dealt with by aspiration The use of a drain favors infection in some degree at least, for it is a foreign body in the wound and it provides a channel of communication between the wound and the outside dressing I recommend more care with hemostasis rather than elaborate arrangements for drainage such as that devised by Raffl

plane, and careful hemostasis Good hemostasis can only be achieved when the surgeon is willing to take care to identify and clamp all visible vessels before cutting them The gentle handling of tissues is also important The late George Crile put it well many years ago when he classified surgeons as the carniverous type who stretch, tear and crush the tissues and the herbivorous type who dissect gently In radical mastectomy broad areas of tissue are exposed and the drying of these tissues must be guarded against by keeping them covered with moist compresses if shock is to be avoided

If despite all these precautions to avoid shock the blood pressure falls un reasonably measures must be taken to bring it up again The blood pressure must not be permitted to remain at a dangerously low level for any considerable length of time. In patients with cardiovascular disease neglect of this precaution courts disaster By following these general principles and no doubt by good fortune, I am able to say that I have had no operative deaths in the series of 553 radical mastectomies for which I have been personally responsible either as the operator or as the first assistant to my resident surgeon

The After Care

Rest for the patient, and an early resumption of fluid and food intake are the immediate objectives of the general postoperative care With the type of anes thesia which I have described our patients are regularly able to take fluids by mouth within a couple of hours after the completion of the operation, and they often tolerate a light meal toward the end of the day Rest is also good for the wound, because it favors good healing. The patient is put in bed on her back but I do not permit her to be turned during the first seventy two hours. Her position may be changed by gatching the head or the foot of the bed up if she desires it. This position is tedious, but since I use morphine or Demerol generously during this period, patients usually do not mind it.

It must be assumed that there has been a degree of bacterial contamination of all wounds in which the operation has lasted a number of hours, and in which skin grafting has been done To avoid infection I therefore give my patients an antibiotic prophylactically for a week after operation I usually use a combina tion of penicillin and streptomycin

I do all the postoperative dressings of my radical mastectomy wounds per sonally I long ago learned that the care of these skin grafted wounds is so com plex that if perfect wound healing is to be achieved I cannot leave the dressings to my house staff I must do them myself I believe moreover that I myself benefit from this experience and that I still continue to learn about wound healing

At the end of seventy two hours, I remove the ace bandages and the fluffed gauze, and inspect the skin graft. If it has been ballooned up anywhere by the accumulations of serum and blood beneath it, I evacuate them. There is no longer any need for a pressure dressing, and I cover the wound merely with several layers of gauze fastened around the periphery with a frame of Elastoplast.

The arm is now free, and I urge the patient to use it for motions of limited extent, such as holding a newspaper and eating I caution her against abducting the arm very much from the chest wall It is certainly very wrong to abduct the

around the chest and arm The hand is left free, protruding between the folds of the ace bandage The whole is securely fastened with safety pins and adhesive

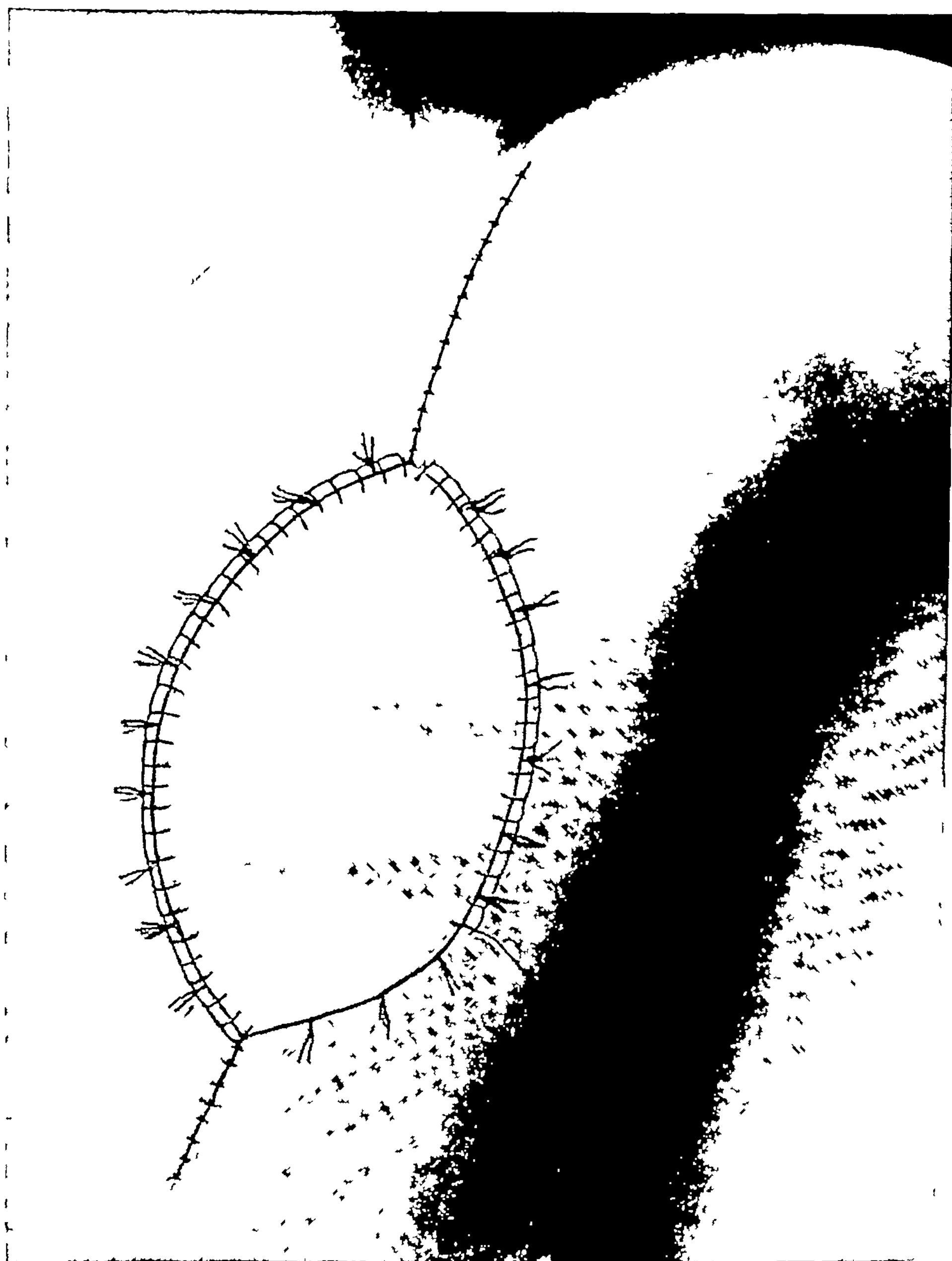


Fig 371 Skin graft sutured in place over defect on chest wall

The Prevention of Shock

An experienced operator, working steadily and rapidly, can complete this operation, including the preliminary biopsy of the tumor itself, in between five and six hours My personal operating time has averaged 308 minutes I take what time I need to perform the dissection that is required I do not operate by the clock, although I do not waste time

Unless precautions are taken to avoid it, shock will sometimes develop in patients operated upon for this length of time The most important of these precautions are the maintenance of the anesthesia on a comparatively superficial

achieved much popularity in this country or indeed anywhere in the world, during the half century since it was devised Its performance demands patience and fortitude and most surgeons are content to do a considerably abbreviated operation It is my hope that the operation will become more popular when it is better known and its advantages in terms of complete local eradication of the carcinoma more fully appreciated My own experience with it has convinced me that it is the best surgical procedure that has been devised for attacking mammary carcinoma in its operable stage It has given me results beyond my expectations which I now wish to present

Principles to be Followed in Reporting Results of Treatment

In any statement of the results of treatment of breast carcinoma there are several basic principles to be followed

I believe that it is important to express results in terms of what we have called the *clinical cure* rate, as well as in terms of the *survival rate* Smithers uses the term *recurrence free* rate to express what we mean by the *clinical cure* rate We both refer to patients who have continued to be free of evidence of persistence or recurrence of their carcinoma from the date of their treatment throughout the whole of the designated period of observation I have called this result *clinical cure* because it clearly indicates that the patient has been continuously well This is a very different status from that which the Subcommittee of the World Health Organization has recommended (1950) as a basis for reporting results Their "apparent recovery rate is based upon the proportion of patients who are alive with no clinical evidence of disease at the designated point in time be it 5 or 10 years They include patients who have developed recurrence and have been treated for it with apparent success, as well as patients who failed to respond to the first planned treatment and have been treated by another method with apparent success.

The *clinical cure* rate is, I believe of great importance in evaluating results because it indicates a kind of therapeutic achievement that is not indicated by the mere survival rate As the efficacy of radiotherapy and of hormone treatment improves, it is apparent that these methods are keeping patients alive, although they are often invalids for long periods of time There is a great difference between a patient with a persisting carcinoma on her chest wall and a badly swollen arm following irradiation for recurrent axillary or supraclavicular metastasis perhaps crippled by metastases in her lumbar vertebrae and a healthy and happy woman with no evidence of disease and an arm that gives her no trouble Both have survived for the designated period of time but what a difference in their fate! The clinical cure rate gives some indication of this difference We have therefore included both the clinical cure rate and the survival rate in reporting our results.

Five years has been generally accepted as the most significant point in time at which to measure the results of treatment of breast carcinoma, and it has much to recommend it. About two-thirds of the patients who eventually develop local recurrence or distant metastases following radical mastectomy do so during the first three years after operation By the time the five year point has been reached the patient can face the future with comparative assurance

patient's arm to a right angle at this stage, as some surgeons in the past have done This motion pulls the axillary flap out away from the chest wall, and hinders obliteration of the dead space in the axilla

After six or seven days I take the dressing down completely for the first time, removing all the sutures around the edge of the graft except two or three of the interrupted sutures holding the axillary portion of the lateral flap down to the chest wall It is wise to leave these few for as long as ten days to avoid the accident of the patient's abducting the arm too far and pulling the lateral flap away from the chest wall

I usually get my patients out of bed on the sixth or seventh postoperative day, and they are usually ready to go home on from the twelfth to the fourteenth day The skin graft donor area on the thigh, also covered originally with Xeroform



Figs 372 and 373 Arm motion following radical mastectomy

gauze, is not dressed until the day of discharge, when it will be found to be healed

By the time the patient goes home, she will be using her arm comparatively freely for limited motions She should now be urged to begin to increase the degree of abduction and to use the arm as normally as possible During the month that follows, a simple exercise which gains abduction gradually is that of abducting both arms together in a transverse plane, with the forearms extended If this motion is practiced several times a day, the full range of arm motion will eventually be regained In achieving this, patients have to bear some discomfort but this is not greater than most will tolerate

The operation which I have described does not cripple the arm Patients are eventually able to use the arm for everything from scrubbing floors to playing tennis Figures 372 and 373 show the absence of any constriction across the axilla in one of my patients

Edema of the arm has always been one of the major hazards of radical mastectomy I will discuss it separately

The true Halsted radical mastectomy which I have here described has not

such absolute data are available Dr Stout and I have reported the Presbyterian Hospital results for breast carcinoma from 1915 to 1942 in this manner Fortunately absolute rates are available from a number of European hospitals

When the results achieved with a particular method of treatment by a single therapist or by a group of therapists utilizing only a selected portion of all the patients with breast carcinoma coming to a hospital are reported they are termed *relative* clinical cure or survival rates Here again no deductions may be made from the selected group of patients Those dying from operation those lost to follow up as well as those dying of intercurrent disease must be counted as dying of cancer These *relative* rates are useful as a method of comparing the value of individual methods of treatment in groups of selected patients The basis on which the patients are selected should of course be stated It is such an accounting of *relative* results that I am able to make regarding my personal series of cases.

Results of Treatment—a Personal Series of Cases

Between the years 1935 and 1950 during which I served as attending surgeon to the Presbyterian Hospital the service chiefs under Dr Whipple s direction assigned a total of 183 patients to me from among the ward patients with breast carcinoma whom I had seen in consultation and for whom I had advised operation The Halsted mastectomies that were done upon these 183 patients were performed by the resident surgeon with me acting as first assistant

During this same period of time I myself performed the operation upon a total of 173 patients whom I selected from among those who came to me privately The total of 356 patients who constitute my personal series of cases are therefore a highly selected group I do not seek to excuse this fact Rather I emphasize it. *My ambition has been to select for radical mastectomy only those patients whom I can cure* As I have already stated I do not wish to perform the *operation on those whom I cannot cure because I am convinced that when operation fails* it is not merely futile—it does harm My results (Table 130) show all too clearly that I am far from achieving my ideal of selecting for operation only curable patients Obviously I can never fully attain it, but I believe that I am learning, albeit slowly how to improve my selection The clinical criteria of operability which I have described in Chapter 26 were the basis for my selection of the 356 cases in my personal series I followed these criteria as strictly as possible

To another surgeon or radiotherapeutist who may say that my results in this personal series of cases were achieved by the selection of favorable cases I reply Go thou and do likewise." My results show what can be accomplished with the kind of radical mastectomy I have described performed in a series of cases of breast carcinoma strictly selected according to criteria which have been defined in great detail If others will but select series of cases by means of the same criteria and treat them uniformly with other methods we can hope to compare the efficacy of their treatment and mine

The essential features of the results in my personal series of 356 radical mastectomies are shown in Table 130 I cannot give any figure for operability because the ward cases were assigned to me at random from a much larger number

Because local recurrence or distant metastasis develops in a small proportion of patients after five years, it is desirable, however, to report 10 year clinical cure and survival rates Approximately 15 per cent of all the patients who develop local recurrence or distant metastasis following radical mastectomy do so during the second five year period *After ten years the probability of dying from intercurrent disease is so high, because patients have reached old age, and the chance of developing late recurrence is so small (only about 1 per cent in our data), that it makes it unprofitable to report longer clinical cure and survival rates The actuarial aspects of this problem have been discussed by Smithers and Stocks, and Berkson and Gage, and it is of no advantage to discuss them here

The necessity of evaluating the long term results of irradiation, however, makes it desirable to extend follow-up of patients treated by irradiation to the 15 and even the 20 year limits We have today very little knowledge of the eventful fate of patients with carcinoma of the breast treated with apparent success by irradiation We know that their carcinomas remain locked up by fibrosis for a long time, but there have not been a large enough number of patients treated adequately with modern irradiation methods and followed for more than 10 years, to enable us to learn much about their later fate

If a statement of results of treatment of breast carcinoma is to be a true expression of the achievement of a particular clinic or hospital in controlling the disease it must be complete It must include data as to the total number of *primary* patients with breast carcinoma admitted to the out-patient, and ward and private bed services of the hospital during a stated period, and the disposition of all *Secondary* cases, namely, those in which curative therapy has previously been given at another hospital, are not properly the responsibility of the hospital to which they subsequently go, usually with recurrent disease The number of these secondary cases should be stated, but their further course need not be reported It should be accounted for in the statement of results by the hospital in which they received their original curative treatment Unless some such division of responsibility for the accounting of results is followed, much duplication and confusion results, at least in our American hospital system where patients are free to change hospitals as they wish

Every significant detail of the subsequent course of all *primary* cases should, however, be recorded All these patients should be followed for the remainder of their lives In calculating the results of treatment no deductions may be made of patients not treated or those treated incompletely, of those in whom microscopical evidence is lacking, of those dying as the result of operation, of those lost to follow-up, or of patients dying of intercurrent disease during the follow-up period The numbers of patients in these various categories should be stated but all must be counted as dying of cancer The fate of all the patients is *determinate* in a statement of results, and no primary cases may be deducted without distorting the truth The clinical cure and survival rates that are derived from complete data of this kind, without any deductions from the total number of primary cases, are appropriately called *absolute* rates They do indeed express the absolute achievement in the control of the disease by the reporting hospital If we are to compare the efficacy of treatment in different hospitals it must be done on the basis of such absolute rates There are only a few American hospitals from which

metastases is shown in Table 132. Local recurrence may be of three types There are the parasternal mound like tumors that are the outward manifestation of metastases to internal mammary nodes They are not properly chargeable to the surgeon in the sense of his having implanted them The second and by far the most frequent type of local recurrence is the nodule in the skin flaps on the chest

Table 131 Results of Radical Mastectomy
(Personal Series, 1935–1950)

Status of patients and stage of disease	No patients	5-year clinical cures		5-year survivals	
		No	Per cent	No	Per cent
Private Patients					
Axillary nodes not involved	85	68	80 0	74	87 1
Axillary nodes involved	88	36	40 9	48	54 5
Total	173	104	60 1	122	70 5
Ward Patients					
Axillary nodes not involved	75	58	77 3	64	85 3
Axillary nodes involved	108	40	37 0	51	47 2
Total	183	98	53 6	115	62 8
Total					
Axillary nodes not involved	160	126	78 8	138	86 2
Axillary nodes involved	196	76	38 8	99	50 5
Total	356	202	56 7	237	66 6

Table 132. Relationship of Local Recurrence to Axillary Involvement (Microscopic)
(Personal Series, 1935–1950)

Total Number of Radical Mastectomies	356
I Disease limited to breast	160, or 44.9%
A Parasternal nodules	7
B. Local recurrence on chest only	0
C. Local recurrence in axilla only	0
D Local recurrence both chest and axilla	0
Total cases with local recurrence	7 or 4 4% of 160
II. Axillary nodes involved	196 or 55 1%
A. Parasternal nodules	10
B Local recurrence on chest only	33
C. Local recurrence in axilla only	2
D Local recurrence both chest and axilla	2
Total cases with local recurrence	47 or 24.0% of 196

wall In general such nodules must result from the implantation in the wound of carcinoma emboli that have escaped from blood vessels or lymphatics cut during the operation, or the implantation of carcinoma cells by instruments or sponges from a focus of carcinoma into which the surgeon has unwittingly carried his dissection The operator is certainly responsible for them Either his operative technique has been faulty or he has erred in choosing to operate upon carcinoma

coming to the hospital The private cases represent, also, only a fraction of those I saw privately in consultation The private operating facilities available to me at the Presbyterian Hospital have been so limited that I can care for only a fraction of the patients who come to me There were no operative deaths and none of these patients have been lost track of The relative five year survival rate is 66 6 per cent, and the relative five year cure rate is 56 7 per cent At the end of 10 years approximately 50 per cent remain alive, and all but 6 per cent are apparently cured

The frequency of axillary involvement in my personal series of cases, and its relationship to the clinical cure and survival rate is shown in Table 131 The

Table 130 Results of Radical Mastectomy
(Personal Cases, 1935–1950 and 1935–1945)

		5-year results 1935–1950		10-year results 1935–1945	
		No	Per cent	No	Per cent
I	Number of radical mastectomies	356	100 0	216	100 0
II	Operative deaths	0			
III	Lost track of before end of period	0		0	
IV	Died of unknown cause before end of period	3	0 8	2	0 9
V	Died of intercurrent disease before end of period	13	3 7	9	4 2
VI	Died of breast carcinoma before end of period	103	28 9	98	45 4
VII	Alive at end of period (relative survival rates)	237	66 6	107	49 5
VIII	Alive without recurrence at end of period (relative clinical cure rates)	202	56 7	95	44 0

axillary lymph nodes were involved in 55 1 per cent of the cases This figure is the best indication of the type of cases included in this personal series They were clearly somewhat less advanced than in our Presbyterian Hospital series of radical mastectomies as a whole, in which 61 6 per cent of the patients had axillary metastases Comparison of my personal series with series from other clinics will show, however, that my series was not an exceptionally favorable one For example, in Dahl-Iversen's "fourth series" of cases which he has recently completed, the axillary lymph nodes were involved in only 41 per cent

A feature of my personal series of cases which I should like to emphasize is that the results were essentially as good in the series of ward patients, where I served as first assistant and the operation was performed by my pupil, the resident surgeon, as they were in my series of private patients where I operated myself This substantiates the point which I have repeatedly emphasized, that the operation in itself, as we do it, is not technically difficult, and that it can be successfully performed by properly instructed surgeons who have not had a great experience with it

The frequency of local recurrence and its relationship to regional lymph node

improved to exclude more of the incurable cases One of the basic factors in prognosis that must not be misunderstood is that of axillary metastasis We tend to assume that any degree of axillary node involvement is catastrophic Table 134 indicates, however that in patients with only either one or two involved axillary nodes, the incidence of local recurrence continues to be very low and the clinical cure rate comparatively high When from 3 to 7 nodes are involved the results are only one half as good and when 8 or more nodes are involved the results are so poor that radical mastectomy can scarcely be justifiable

Table 134 Results of Radical Mastectomy in Patients with Involved Axillary Nodes
(Personal Series, 1935–1950)

No of nodes microscopically involved	No of cases	5-yr local recurrences			5-yr clin cures		5-yr survivals	
		Parasternodules	Local recur	Per cent	No	Per cent	No	Per cent
1–2	67	2	3	7 5	44	65 7	50	74 6
3–7	62	5	8	21 0	23	37 1	33	53 2
8 or more	61	3	26	47 5	9	14 8	16	26 2
Total cases	190	10	37	24 7	76	40 0	99	52 1

Table 135 Results of Radical Mastectomy Related to Preoperative Clinical Findings
(Personal Series, 1935–1950)

Clinical findings	No of cases	No Axill. met.	Axill. met	5-yr local recurrences			5-yr clin. cure		5-yr survivals	
				Paraster nodules	Local recur	Per cent	No	Per cent	No	Per cent
A. Nodes not clin. inv no grave signs	181	119	62	8	6	7 7	135	74 6	153	84 5
B. Nodes clin. inv no grave signs	107	24	83	5	15	18 7	53	49 5	64	59 8
C. One or more grave signs	55	10	45	4	16	36 4	14	25 5	20	36 4

We have of course no way of knowing the extent of microscopical axillary metastases in these terms before operation These facts can not therefore be used as criteria of operability

In search of more strict clinical criteria of operability in my series of personal cases Dr Cooley and I have sorted out the cases in various ways The simplest and at the same time the most discriminating, classification based on clinical features that we have found is that shown in Table 135 Cases in Group A include those with no clinically involved axillary nodes and none of the five grave signs

so far advanced that it is impossible to get it all out This same criticism applies when there is recurrence in the axilla

Although most recurrent nodules on the chest wall are distressingly genuine, the possibility of pseudo-recurrence must always be kept in mind Foreign body cysts around suture material sometimes simulate true recurrence, as described by Moschowitz Another form of pseudo-recurrence is the bony hard, fixed nodule that develops on a rib or costal cartilage where the surgeon's knife has nicked it These prove to be merely proliferation of periosteum or perichondrium

In my personal series of cases in which there were no axillary metastases I achieved my ambition of no local recurrence in the skin flaps on the chest wall or in the axilla The seven parasternal recurrences could not have been avoided

Table 133. Frequency and Distribution of Local Recurrences and Metastases within Five Years Following Radical Mastectomy

(Personal Series, 1935–1950)

I	Total number of radical mastectomies	356
II	Number known to develop local recurrence within 5 years after operation	54, or 15 2%
	A Parasternal nodules	17, or 4 8%
	B In the operative field on the chest wall	35, or 9 8%
	C In the homolateral axilla	4, or 1 1%
III	Number developing metastases in known sites within 5 years after operation	129, or 36 2%
	A In lung or pleura	61, or 17 1%
	B In bone	52, or 14 6%
	C In supraclavicular regions	31, or 8 7%
	D In liver or peritoneum	22, or 6 2%
	E In opposite breast	9, or 2 5%
	F In contralateral axilla	12, or 3 4%
	G In regional skin, or as en cuirasse	12, or 3 4%
	H Distant skin metastases	9, or 2 5%
	I In other sites	37, or 10 4%

In the cases with axillary metastases in my personal series, however, I failed badly in terms of local recurrence of the disease in the skin flaps This occurred in 18 per cent of my patients It is remarkable, however, that only 4 of these 196 patients with axillary metastases developed local recurrence in the axilla These facts mean that my criteria of operability regarding the local extent of the primary carcinoma have not been strict enough, and that I must narrow them My criteria of operability in terms of axillary involvement, on the other hand, seem to have been correct

The frequency of local recurrence in my personal series of cases is compared with the frequency of distant metastases to various sites in Table 133 There is nothing remarkable about the distribution of the distant metastases in my series of cases Metastases to lungs or pleura, bone, the supraclavicular region, and the liver head the list, in the order named

Studying these results in my personal series of radical mastectomies, in which the patients were selected on the basis of our clinical criteria of operability, Dr Cooley, my statistician associate and I, have wondered how the selection might be

The 5 year results, according to the method of treatment used are shown in Table 139

The 5-and 10-year results of radical mastectomy are shown in Table 140 These results differ very slightly from those presented in the report Dr Stout and I published in 1951 This difference is due to our recently finding five patients to be alive and well whom we had previously lost track of and counted as dead of carcinoma

Table 137 Disposition of Cases
(Presbyterian Hospital 1935–1942)

I Patients previously treated elsewhere		119
A No further treatment by surgery or radiation		49
B Further treatment by radiation		57
C. Further treatment by surgery		13
1 Palliative limited operation	11	
2. Radical mastectomy	2	
II. Primary cases		668
A Not treated by surgery or radiation		37
B Treated by radiation only		107
C Treated principally or exclusively by surgery		524
1 Irradiation followed by simple mastectomy	4	
2. Local excision or partial mastectomy	5	
3 Simple mastectomy	13	
4 Simple mastectomy plus axillary dissection	7	
5 Radical mastectomy	495	

Table 138. Classification of Primary Cases Not Treated by Radical Mastectomy
(Presbyterian Hospital 1935–1942)

I. Constitutionally inoperable (9 of these also inoperable because of extent of carcinoma)	36
II Inoperable because of extent of carcinoma	123
III. Refused radical mastectomy	10
IV Referred elsewhere because of lack of accommodations	1
V Carcinoma mistaken for benign lesion and radical mastectomy not done	3
Total	173

Table 139 Five Year Results According to Method of Treatment Primary Cases
(Presbyterian Hospital, 1935–1942)

Method of treatment	Cases	5-year clinical cure	5-year survival
No treatment	37	0	0
Irradiation only	107	9	17
Irradiation followed by simple mastectomy	4	0	1
Local excision or partial mastectomy	5	1	1
Simple mastectomy	13	2	3
Simple mastectomy plus axillary dissection	7	5	5
Radical mastectomy	495	246	293
Totals	668	263	320

of locally advanced carcinoma The five grave signs are the same ones that I have referred to in Chapter 26

1 Ulceration
2 Edema of limited extent
3 Solid fixation of the tumor
4 Axillary nodes 2 5 cm or more in transverse diameter
5 Fixed axillary nodes

Group A has a satisfactorily low local recurrence rate and a clinical cure rate of approximately 75 per cent This group nevertheless included 34 per cent of cases with axillary metastases

Cases in Group B, with clinically involved nodes but no grave signs of locally advanced carcinoma, gave results close to the average for my entire series

Cases in Group C, with one or more of the five grave signs of locally advanced disease, gave results which were very disappointing—36 per cent of local recurrence and only 25 5 per cent of 5 year clinical cures

It must be remembered in interpreting the significance of this classification that all these cases in my personal series had already passed the selective test of our clinical criteria of operability as defined in Chapter 26 The classification in Table 135 is an additional refinement of clinical selection It suggests a method by which surgeons who wish to limit operability still more by purely clinical criteria may do so It indicates further, that since the five grave signs of locally advanced disease seem to be the weightiest factor in prognosis, that where we need to narrow our clinical criteria of operability is in terms of the local extent of the primary tumor

Results of Treatment—Presbyterian Hospital Series of Cases

In contrast to my personal series of cases for which I can present only *relative* results, I can present *absolute* results for our Presbyterian Hospital series of cases I have chosen to present those for the period 1935–1942 because the data are more complete than for earlier years

The records of all women with proved or presumed carcinoma of the breast coming to the out-patient, ward, and private beds of the Presbyterian Hospital between the years 1935 to 1942, inclusive, are included in Table 136

The disposition of our Presbyterian Hospital cases is shown in Table 137

There were a total of 173 primary cases in which radical mastectomy was not done The reasons for not operating are detailed in Table 138

Table 136 Carcinoma of the Female Mammary Gland
(Presbyterian Hospital, 1935–1942)

Total number of patients applying for treatment	787
A Previously treated elsewhere	119
B Primary cases	668
1 Private cases	257
2 Ward cases	411

The 5 year results according to the method of treatment used are shown in Table 139

The 5-and 10-year results of radical mastectomy are shown in Table 140 These results differ very slightly from those presented in the report Dr Stout and I published in 1951 This difference is due to our recently finding five patients to be alive and well whom we had previously lost track of and counted as dead of carcinoma

Table 137 Disposition of Cases
(Presbyterian Hospital, 1935–1942)

I Patients previously treated elsewhere		119
A. No further treatment by surgery or radiation		49
B Further treatment by radiation		57
C. Further treatment by surgery		13
1 Palliative limited operation	11	
2. Radical mastectomy	2	
II Primary cases		668
A Not treated by surgery or radiation		37
B Treated by radiation only		107
C. Treated principally or exclusively by surgery		524
1 Irradiation followed by simple mastectomy	4	
2. Local excision or partial mastectomy	5	
3 Simple mastectomy	13	
4 Simple mastectomy plus axillary dissection	7	
5 Radical mastectomy	495	

Table 138. Classification of Primary Cases Not Treated by Radical Mastectomy
(Presbyterian Hospital, 1935–1942)

I Constitutionally inoperable (9 of these also inoperable because of extent of carcinoma)	36
II Inoperable because of extent of carcinoma	123
III. Refused radical mastectomy	10
IV Referred elsewhere because of lack of accommodations	1
V Carcinoma mistaken for benign lesion and radical mastectomy not done	3
Total	173

Table 139 Five Year Results According to Method of Treatment Primary Cases
(Presbyterian Hospital, 1935–1942)

Method of treatment	Cases	5-year clinical cure	5-year survival
No treatment	37	0	0
Irradiation only	107	9	17
Irradiation followed by simple mastectomy	4	0	1
Local excision or partial mastectomy	5	1	1
Simple mastectomy	13	2	3
Simple mastectomy plus axillary dissection	7	5	5
Radical mastectomy	495	246	293
Totals	668	263	320

Table 140. Results of Radical Mastectomy
(Presbyterian Hospital, 1935–1942)

	5-year results		10-year results	
	Number cases	Per cent	Number cases	Per cent
I Radical mastectomies performed	495	100 0	495	100 0
II Operative deaths	9	1 8	9	1 8
III Lost track of before end of period (ward 3, private 15)	14	2 8	18	3 6
IV Died of unknown cause before end of period	7	1 4	7	1 4
V Died of intercurrent disease before end of period	18	3 6	30	6 1
VI Died of breast carcinoma before end of period	154	31 1	222	44 8
VII Alive at end of period (relative survival rates)	293	59 2	210	42 4
VIII Alive without recurrence at end of period (relative clinical cure rate)	246	49 7	186	37 6

The *absolute* survival and clinical cure rates computed in these Presbyterian Hospital data are shown in Table 141 It should be emphasized again, in presenting these rates, that no deductions of any kind have been made from the total number of primary cases of carcinoma of the breast coming to the hospital during the period 1935–1942

It is informative to present the *absolute* and *relative* survival rates year by year, as Smithers has done The absolute rates represent survival of all primary car-

Table 141 Absolute Survival and Cure Rates Following Radical Mastectomy
(Presbyterian Hospital, 1935–1942)

	5-year	10-year
Absolute survival rates (number of survivals — Total no of primary cases, or $\frac{320}{668}$ and $\frac{223}{668}$)	47 9	33 4
Absolute clinical cure rates (number of clinical cures — Total no of primary cases, or $\frac{263}{668}$ and $\frac{186}{668}$)	39 4	27 8

cinoma patients, while the relative rates represent survival of treated patients only These have been calculated, following Smithers, in two ways The minimum rates are based on the assumption that all untraced patients died of carcinoma, while the maximum rates are based on the assumption that all untraced patients are alive Table 142 reproduces Smithers' rates for the Royal Cancer Hospital, and adds those achieved in the Presbyterian Hospital, from one to fifteen years after admission

The frequency of local recurrence following radical mastectomy and its relationship to regional lymph node metastases is seen in Table 143 Again as in my personal series of cases it is encouraging that the frequency of local recurrence is exceedingly low in the patients without axillary metastases

Table 142. Annual Survival Rates for Carcinoma of the Breast

	Royal Cancer Hospital (after Smithers) 1937–1948		Presbyterian Hospital 1935–1942	
Years after admission	Minimum	Maximum	Minimum	Maximum
		Absolute Survival Rates (all primary patients)		
1	72 4	76 7	80 5	82 5
2	55 0	60 2	68 4	70 3
3	44 6	51 1	59 6	61 5
4	38 2	44 9	54 0	56 0
5	34 6	41 8	47 8	49 7
7	26 7	34 5	39 7	42 1
10	20 7	31 0	33 4	36 1
15			16 9	29 5
		Relative Survival Rates (All patients treated by all methods)		
1	75 3	79 8	85 3	87 3
2	57 0	62 4	72 4	74 5
3	46 1	52 8	63 1	65 1
4	39 3	46 1	57 2	59 3
5	35 4	42 8	50 6	52 6
7	27 2	35 1	42 0	44 5
10	21 2	31 7	35 5	38 2
15			17 8	31 1
		Relative Survival Rates (Patients treated by radical mastectomy)		
1			90 3	92 2
2			80 6	83 2
3			72 1	74 7
4			66 9	69 5
5			59 4	62 0
7			49 7	52 9
10			42 6	46 1
15			21 7	39 2

Table 144 shows the frequency of local recurrence following radical mastectomy in comparison with that of metastasis to various distant sites in the Presbyterian Hospital data.

Types of Radical Mastectomy The 495 radical mastectomies in the present series were performed by or under the direction of a score of attending surgeons There was great variation in their operative techniques Two main types of operation however were done

Table 143 Relationship of Local Recurrence to Axillary Involvement (Microscopic)
(Presbyterian Hospital, 1935–1942)

Total number of radical mastectomies		495
I Disease limited to breast		190, or 38 3%
A Parasternal nodules	1	
B Local recurrence on chest only	4	
C Local recurrence in axilla only	0	
D Local recurrence both chest and axilla	0	
Total cases with local recurrence	5, or 2 6% of 190	
II Axillary nodes involved		305, or 61 6%
A Parasternal nodules	8	
B Local recurrence on chest only	40	
C Local recurrence in axilla only	3	
D Local recurrence both chest and axilla	8	
Total cases with local recurrence	59, or 19 3% of 305	

1 *Radical Mastectomy—Skin Flaps Approximated without Grafting* This operation approximated the standard American radical mastectomy The amount of skin removed was limited by the necessity of bringing the flaps together The flaps were, moreover, usually cut so thick that they would tolerate rough handling and considerable tension

Table 144 Frequency and Distribution of Local Recurrence and Metastases within Five Years Following Radical Mastectomy in Primary Cases
(Presbyterian Hospital, 1935–1942)

I Total number of radical mastectomies		495
II Number known to develop local recurrence within 5 years after operation		64, or 12 9%
A Parasternal nodules	9, or 1 8%	
B In the operative field on the chest wall	52, or 10 5%	
C In the homolateral axilla	11, or 2 2%	
III Number developing metastases in known sites within 5 years after operation		189, or 38 2%
A In lung or pleura	94, or 19 0%	
B In bone	91, or 18 4%	
C In supraclavicular regions	39, or 7 9%	
D In liver or peritoneum	27, or 5 4%	
E In opposite breast	24, or 4 8%	
F In contralateral axilla	12, or 2 4%	
G In regional skin, or as en cuirasse	12, or 2 4%	
H Distant skin metastases	12, or 2 4%	
I In other sites	36, or 7 3%	

2 *Radical Mastectomy—Wound Grafted* This was a more radical procedure, particularly as regards removal of skin and subcutaneous tissue on the chest wall The skin defect was covered by a Thiersch graft This operation approximated the classical Halsted mastectomy

A comparison of the results obtained with these two different types of so-called radical mastectomy (Table 145) does not seem to show any significant superiority of the Halsted operation From my own knowledge of the reasoning

Table 145 Results in Different Types of Radical Mastectomy in Primary Cases
(Presbyterian Hospital, 1935–1942)

Type of operation	Number of cases	Operative deaths		5-year local recurrence		5-year clin. cures	
		No	Per cent	No	Per cent	No	Per cent
I. Limited to radical—pectoralis minor not removed	2	0	—	0	—	1	—
II. Radical—breast and axillary contents removed separately	5	1	—	1	—	3	—
III. Radical—skin flaps approximated without grafting	214	6	2 8	21	9 8	100	47 7
IV Radical—wound grafted	274	2	0 8	42	15 3	140	51 1
Totals	495	9	1 8	64	12 9	246	49 7

of many of the surgeons who performed these operations however I know that they usually did skin grafts only in the more advanced cases in which they felt it was necessary to sacrifice more skin over the breast The incidence of axillary metastases in the cases in which skin grafting was not done was 59 3 per cent. In the cases in which grafting was done (excluding my own cases which were always grafted) the incidence of axillary metastases was 65 7 per cent.

There has been a tendency among our surgeons during recent years to perform the more radical type of operation with skin grafting in all cases of breast carcinoma This is indicated in Table 146 where the cases in both our earlier and

Table 146. Length of Radical Mastectomy in Primary Cases According to Five-Year Periods.
(Presbyterian Hospital)

Length of operation in minutes	No of cases 1915–1919	No of cases 1920–1924	No of cases 1925–1929	No of cases 1930–1934	No of cases 1935–1939	No of cases 1940–1942
0– 59	28	15	11	2	0	0
60–119	65	52	81	57	14	3
120–179	32	58	60	89	63	11
180–239	2	2	6	61	110	35
240 or more	0	0	1	15	127	132
Time not stated	1	0	1	1	0	0
Totals	128	127	160	225	314	181

our recent series are grouped in quinquennial periods according to the length of time required for the operation It will be seen from this table that in our earlier 1915–1934 series the surgeon devoted three or more hours to the operation in only 13 6 per cent of the cases But in the present 1935–1942 series of cases 80.2 per cent of the radical mastectomies lasted three hours or more When the length of time devoted to radical mastectomy is correlated with the end results as shown in Table 147 there is suggestive evidence that the results improve with the length of time devoted to the operation

Table 147. Results of Radical Mastectomy in Primary Cases According to Length of Operation
(Presbyterian Hospital, 1935–1942)

Length of operation in minutes	Number of cases	Operative deaths No.	Operative deaths Per cent	5-yr local rec. No.	5-yr local rec. Per cent	5-yr clinical cures No.	5-yr clinical cures Per cent
I 60 to 119	17	1	5.9	3	17.6	4	23.5
II 120 to 179	74	2	2.7	10	13.5	34	45.9
III 180 to 239	145	2	1.4	18	12.4	68	46.9
IV 240 to 299	142	4	2.8	18	12.7	73	51.4
V 300 or more	117	0	0	15	12.8	67	57.3
Totals	495	9	1.8	64	12.9	246	49.7

When our Presbyterian Hospital data are reviewed in quinquennial periods beginning in 1915, as in Table 148, it will be seen that there has been a steady diminution in the local recurrence rate and a corresponding rise in the clinical cure rate. This improvement is of course largely explained by the increasingly critical selection of cases for operation, but I believe that it is due at least in part to the adoption of a more radical surgical attack embodying the principle of a more extensive sacrifice of skin over the breast, the dissection of thin skin flaps, the use of a skin graft to cover the defect, and to the willingness of the surgeons to devote more time and care to the operation.

Table 148. Results of Radical Mastectomy by Quinquennial Periods
(Presbyterian Hospital, 1915–1942)

Five year periods	Number of operations	Operative deaths No.	Operative deaths Per cent	5-yr local recurrence No.	5-yr local recurrence Per cent	5-yr clinical cures No.	5-yr clinical cures Per cent
I 1915–1919	128	3	2.3	32	25.0	34	26.6
II 1920–1924	127	7	5.5	24	18.9	37	29.1
III 1925–1929	160	8	5.0	42	26.3	53	33.1
IV 1930–1934	225	2	0.9	48	21.3	107	47.6
V 1935–1939	314	5	1.6	44	14.0	148	47.1
VI 1940–1942	181	4	2.2	20	11.0	98	54.1

Local Recurrence in Relation to Skin Grafting

One of the controversial questions regarding the technique of radical mastectomy continues to be whether or not skin grafting is desirable. Halsted, in his 1912 paper describing the method of skin grafting which he had regularly employed for sixteen years, concluded, "It is better to remove too much skin than too little, for the mistake of excising an insufficient quantity is quite fatal to the patient's chance of recovery."

The opposite view was held by Sampson Handley, who wrote in 1906, "The area of skin taken away in the operation should obviously be no larger than necessary, and no healthy skin should be removed. It has already been shown that cancer does not spread in the plane of the skin. . . . The necessary conditions can usually be fulfilled by the removal of a circular area of skin 4 or 5 inches in diameter, with the growth at its center."

It is Handley's point of view that has won out in the half century that has gone by since these two distinguished students of breast carcinoma disagreed Today the standard American radical mastectomy sacrifices so little skin that the flaps can be brought together albeit with some tension Skin grafting has been abandoned even by most of the pupils of Halsted's pupils There are only a very limited number of surgeons who continue to graft skin regularly

The first point to be noted regarding skin grafting is that it is impossible to find solid statistical evidence proving that the results of radical mastectomy without skin grafting are inferior For example at the Massachusetts General Hospital a general hospital where as at the Presbyterian Hospital there has been special emphasis upon the problem of breast carcinoma and where the follow up data are very complete, the frequency of local recurrence in the most recently reported case series (1936–1941) according to Taylor is 11 per cent Skin grafting is infrequently done At the Presbyterian Hospital where in recent years most of the operations have included skin grafting, the incidence of skin recurrence in the 1940–1942 (Table 148) series of cases was precisely the same—11 per cent.

In a paper on the subject which he wrote in 1946 White compared the frequency of local recurrence in a number of clinics without being able to demonstrate any advantage in skin grafting. He quite rightly concluded, however that local recurrence after radical mastectomy is a distressingly common experience in all clinics

Conway and Neumann subsequently made a detailed study of the relationship of local recurrence to skin grafting in 255 radical mastectomies performed at the New York Hospital between 1932 and 1942 Although they found that the recurrence rate was actually higher in the grafted cases, these cases had a higher incidence of axillary metastases and were therefore presumably more advanced One worthwhile correlation emerged from their study—it was that the frequency of local recurrence increased with the size of the primary tumor

Despite a lack of statistical evidence I am still convinced of the desirability of sacrificing so much skin over the breast that a graft must be used I see in consultation many patients with nodular recurrence in the skin flaps, often along the suture line, in whom it is obvious that not much skin was sacrificed Some of these are patients in whom the carcinoma was not advanced. Now I must at once admit that my own chest wall local recurrence rate is distressingly high—9 8 per cent But my local recurrences do not occur in early cases, and they do not crop up along the suture line They appear out in the width of the flaps They develop in patients whose disease was locally more advanced than my clinical estimate led me to believe. They must be due to implantation in the wide reaches of the operative field on the chest wall of carcinoma emboli that have escaped from the subdermal lymphatics, or from minute foci of carcinoma in the most superficial portion of the breast parenchyma They are clearly the result of my blundering into operating upon carcinoma that is locally inoperable My criteria of operability in terms of the local extent of the disease are not strict enough

I wish however to preserve my good record of a low local recurrence rate in the earlier cases and to be certain of this it seems safer to continue to sacrifice skin generously

A second reason why I intend to continue skin grafting is that I am convinced

that it is a kindness to the patient, quite apart from the matter of local recurrence One advantage of skin grafting is that it saves the patient discomfort If the skin flaps are not sutured with tension it is amazing to me how painless radical mastectomy usually is My patients often tell me they have had no pain at all postoperatively On the other hand, I see many patients whose skin flaps have been pulled together with tension sutures, and who have had a good deal of pain as a consequence The sensation of constriction of the chest that all patients have to some degree for a considerable time after radical mastectomy is much more marked in patients whose skin flaps have been sutured under tension

A third reason that impels me to suture the skin flaps without tension and to graft skin is that I know that this is the easiest way to make certain of perfect wound healing and to avoid edema of the arm Necrosis, infection, and fibrosis are the triad that lead to edema of the arm, and they are unfortunately frequent when the skin flaps are pulled together under tension

The Time of Recurrence. It is important to look into the question of the time of appearance of local recurrence and distant metastases following treatment of carcinoma of the breast for two reasons The first has to do with the possibility that surgery, when it does not succeed in removing the local disease in its entirety, may disseminate it and accelerate its course I have already presented, in Chapter 26, suggestive evidence in terms of the survival time following operation, that this is indeed a fact Further evidence bearing on this question may be derived from comparison of the time of recurrence in cases treated by surgery with the time of recurrence in those treated solely by irradiation In the Presbyterian Hospital series we do not have enough patients treated solely by irradiation to provide significant data on this point Our Presbyterian Hospital data concerning the time of local recurrence and metastasis following radical mastectomy, however, are shown in Table 149 The total number of recurrences and metastases of the different types (not the first recurrences or metastases) are recorded in this table The cases are divided into three stages, those without axillary metastasis, those with axillary metastasis, and those judged inoperable by our clinical criteria but nevertheless operated upon

It will be seen that the proportions of recurrences and metastases developing during the first three years after operation increased as the stage of the disease at the time of operation advanced Although only about one-half of the recurrences and metastases in the early cases without axillary involvement occurred during the first three years, about nine-tenths of the recurrences and metastases in the late inoperable cases occurred during the first three years This difference might be explained as being due merely to the fact that the carcinomas in the more advanced stage had already begun to advance more rapidly when they were operated upon But if it is assumed that the rate of progression of carcinoma is a constant one, then one is tempted to conclude that operation, when it was performed upon advanced carcinoma, accelerated its course

Smithers and Rigby-Jones found, in the data of the Royal Cancer Hospital, similar evidence of acceleration of the recurrence rate following treatment in the more advanced stages of carcinoma

A second reason for studying the time of appearance of recurrence is that it gives us a clear concept of how late carcinoma may recur, and how frequent

these late recurrences are Those who are inclined toward an easy pessimism like the Mortons argue that since recurrence *may* occur many years after treatment, we cannot speak of curing carcinoma of the breast but only of survival after treatment

Rather than accepting late recurrence as a frequent phenomenon and as one which denies us the right to regard our success with carcinoma of the breast as permanent cure, it is important to look critically into the genuineness of presumed late recurrence. Many of the case reports are so incomplete that no definite conclusion can be drawn from them It is more than likely that rather

Table 149 Year of Appearance Following Radical Mastectomy of Local Skin Recurrences, Metastases to Regional Lymph Nodes to Lungs or Pleura and to Bone in 528 Patients
(First Treated t the Presbyteria Hospital, 1915–1942)

Site of recurrent carcinoma and stage of disease at operation	1st year	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	Later
Local skin recurrences											
Disease limited to breast	5	5	3	1	2	—		1	2	—	1
Axillary nodes involved	41	30	18	6	5	5	1	4	1	—	1
Inoperable	32	12	1	—	2	—	—	—	—	—	—
Totals	78	47	22	7	9	5	3	5	3	—	2
Regional lymph node metastases											
Disease limited to breast	3	6	3	—	5	1	1	—	—	—	1
Axillary nodes involved	47	33	16	8	4	3	2	1	4	3	3
Inoperable	32	8	4	2	1	—	—	—	—	—	—
Totals	82	47	23	10	10	4	3	1	4	3	4
Lung and pleural metastases											
Disease limited to breast	11	10	8	2	4	1	4	4	4	1	1
Axillary nodes involved	25	38	23	22	17	10	4	4	4	3	7
Inoperable	22	22	7	3	2	—	3	—	—	—	—
Totals	58	70	38	27	23	11	11	8	8	4	8
Bone metastases											
Disease limited to breast	5	6	7	3	5	3	2	2	1	2	—
Axillary nodes involved	44	38	24	14	17	9	6	—	1	2	5
Inoperable	22	9	2	2	1	2	—	—	—	—	—
Totals	71	53	33	19	23	14	8	2	2	4	5

than being examples of true late recurrence, they represent one of three other phenomena as follows

(*1*) *The persistence rather than recurrence of carcinoma* It is well established that breast carcinoma occasionally progresses exceedingly slowly I have described such a case in Chapter 19 Another group of patients in this class are those who repeatedly develop recurrences which are controlled by irradiation over a period of many years Patients whose carcinoma has been locked up by irradiation fibrosis until it finally begins to grow again also belong in this category Since these patients are never free from disease it is not proper to classify them as having late recurrence

(*2*) *Metastasis from a different primary carcinoma* In patients who develop metastasis after a long period of freedom from evidence of their disease it is often not certain that the source is the original breast carcinoma It may be a different and occult primary carcinoma Small primary carcinomas from the

lung and pancreas are particularly likely to be missed clinically, and they may closely resemble breast carcinoma microscopically The metastasis may be from a small and undetected primary carcinoma in the second breast The following is a case of this kind which only the autopsy findings saved us from mistaking for an example of late recurrence

Miss H M , aged 44, came to the Presbyterian Hospital in June 1940 complaining of a tumor of the left breast of one month's duration The tumor was situated in the upper inner sector of the breast and measured 7 cm in diameter It was hard, irregularly nodular, and fairly well delimited It was freely movable There was a broad area of dimpling in the skin caudad to it, but no other skin changes In the left axilla there were several nodes up to 1 cm in diameter, and one of them was hard Radical mastectomy was performed There was no involvement of axillary nodes

She was well for 14 and one-half years, until January, 1955, when she developed symptoms of *right* sided pleural effusion X-ray examinations showed massive right pleural effusion There was no evidence of local recurrence of her left mammary carcinoma Careful search revealed no evidence of a new primary carcinoma anywhere else The right breast was normal on palpation She was treated with thoracentesis and estrogens, and survived another year, dying Feb 16, 1956 Autopsy revealed an entirely unsuspected 1 cm carcinoma situated deep in the center of the right breast, which had metastasized to the right pleural cavity, the liver, the diaphragm, the spine, the thyroid, and to right cervical lymph nodes There was no evidence of recurrence of her original left-sided mammary carcinoma It was assumed that the carcinoma in the right breast was a new and independent lesion

An autopsy is always necessary to settle the question of the origin of metastases definitively Willis described one of the best examples of late metastasis proved by autopsy In his case signs of a brain lesion developed 14 years after radical mastectomy for carcinoma At craniotomy a partly calcified, partly cystic metastasis was found in the parietal area of the brain The patient died a week later and other metastases, seemingly from the original breast carcinoma, were found elsewhere in the brain as well as in the hilar region of both lungs, and in the mediastinal lymph nodes No other primary carcinoma was demonstrated

(3) *New primary mammary carcinoma developing from mammary tissue left on thick skin flaps* As I have already pointed out, the skin flaps of the standard American radical mastectomy are so thick that they often include a good deal of mammary tissue It is likely that carcinoma reappearing in the flaps a long time after operation is sometimes a new primary lesion, arising in the residual mammary tissue Wawro has recently described a convincing example of this phenomenon In his patient the new primary developed in breast tissue left on a skin flap from 2 to 4 cm thick, 17 years after the original operation

There have been a good many individual case reports of the late development of local recurrence or distant metastases These reports have recently been tabulated by the Mortons In the data of two of the largest German radiotherapeutic clinics, Bohlig and Bade studied the frequency of recurrence developing later than five years after treatment Bade reported that 2 6 per cent of his patients developed late recurrence defined in these terms, and Bohlig 7 per cent A more complete and careful follow-up of a series of cases of breast carcinomas, such as our Presbyterian Hospital series, will show an appreciably higher incidence of late recurrence Our data as to site and time of appearance of local recurrence

following radical mastectomy shown in Chart 22 give a graphic impression of the phenomenon of recurrence It should be emphasized that this chart shows the actual number of local recurrences and metastases which are often multiple in the same patient. It does not indicate the first recurrence or the number of patients who had recurrence The number of patients who had recurrence is considerably smaller After ten years the number of patients developing recurrence for the first time is very small indeed In our series of 1115 patients treated by radical mastectomy concerning whom we have information as to the site of recurrence, only 13 developed local recurrence or metastasis for the first time after 10 years—that is, 1 1 per cent In two patients there was local recurrence

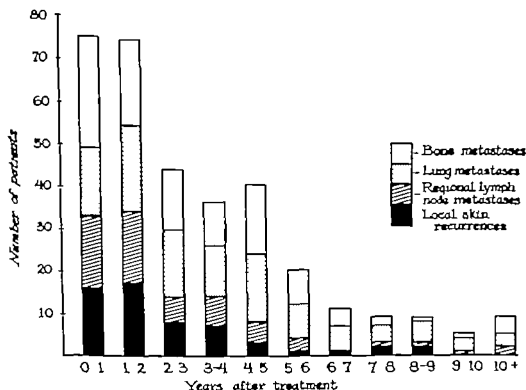


Chart 22. Site and time of recurrence of carcinoma following radical mastectomy (Presbyterian Hospital 1935–1942)

in the skin on the chest wall in one axillary recurrence, in three supraclavicular metastases, in two pulmonary metastases, and in five metastases to bone.

Some of the details of the case histories of these patients of ours with late recurrence are listed in Table 150

Our two cases in which carcinoma recurred in the skin flaps 10 8 and 13.2 years, respectively postoperatively may very well have been like Wawro s case, examples of new primary carcinoma developing in residual mammary gland on the skin flaps In both of these cases the flaps had been cut several centimeters thick.

Our cases with late axillary and supraclavicular metastases may well represent true late recurrence of the original carcinoma. In these four cases the disease reappeared in the regional lymph node filter outside the breast area All four were favorable microscopical types of carcinoma which might be expected to

Table 150 First Recurrence of Breast Carcinoma More than 10 Years after Radical Mastectomy
(Presbyterian Hospital, 1915–1942)

Case no	Patient	Age	Date oper	Skin graft	Axil met	Microscop type	Site of recurrence	Interval operation to recurrence	Autopsy
							LOCAL RECURRENCE IN SKIN FLAPS ON CHEST WALL		
1	A F	55	Feb '27	0	0	Grade II	4 nodules in skin along scar	10 8 years	0
2	E S	58	Feb '27	0	+	Grade II	Nodule near lower end mesial flap	13 2 years	0
							AXILLARY METASTASES		
3	M T	50	Feb '34	0	+	Grade I	Axillary mass	14 years	0
							SUPRACLAVICULAR METASTASES		
4	E I	49	Dec '38	0	+	Circum	Supraclavicular node	10 1 years	0
5	J R	40	Mar '38	0	+	Papillary	Supraclavicular & cervical nodes	10 7 years	0
6	M G	44	Nov '28	0	0	Grade I	Brachial plexus involvement	20 years	0

PULMONARY METASTASES									
7	N P	50	Feb. 42	+	+	Grade II	Lung and pleura	11 8 years	0
8	R.S	44	Nov '23	0	+	Grade I	Lung and pleura	21 3 years	0
BONE METASTASES									
9	A.K.	50	Feb 37	0	+	Grade I	Ribs	10 6 years	0
10	D.L.	38	June 38	0	+	Intraduct.	Femur	11 3 years	0
11	L.B	47	June 37	0	+	Mucoid	Femur	11 5 years	0
12	E.H	48	Apr 37	0	+	Grade I	Femur	11 5 years	0
13	E.H	47	July '21	0	+	Grade II	Generalized in skeleton	14 5 years	0

grow slowly In the three cases in which the metastases were biopsied they were of the same well differentiated types as the primary lesions

The most remarkable of these four cases was that of M G, Case No 6 When she came to the Presbyterian Hospital she had been aware of a tumor in her left breast for two years There was a transverse depression across the upper outer sector of the breast, extending around the edge of the anterior pectoral fold The skin in the depression was reddened Beneath it there was a firm, irregular tumor 3 cm in diameter It was freely movable over the underlying pectoral muscle There were no palpable axillary nodes

Radical mastectomy was done without skin grafting The tumor proved to be a well differentiated Grade I carcinoma that had not metastasized to the axillary nodes

Her first symptom of recurrent disease was pain and numbness in the left hand which began twenty years after her operation A deep hard fullness was noted in the supraclavicular region The arm became edematous The pain increased in severity and extended up the arm into the neck Flaccid paralysis of the arm developed The supraclavicular area was finally explored and extensive carcinomatous involvement of the brachial plexus found This lesion resembled the original primary breast carcinoma microscopically She died two and one-half years after her first symptom of supraclavicular metastasis

Both of our cases of presumed late metastasis to the lung, and 5 cases of presumed metastasis to bone, lack confirmation by autopsy One feature that suggests that they may be genuine late metastases is the fact that five were favorable microscopical types which might be expected to progress slowly Three were Grade I carcinoma, one was a mucoid carcinoma, and the fifth a well differentiated intraductal carcinoma

This latter case, No 8, that of R S, was the most impressive in our series of presumed late distant metastases

She had first noted a tumor in her right breast in November, 1922, a year before she was admitted to the Presbyterian Hospital Examination showed a typical 2 cm carcinoma of the upper outer sector of the breast There were several enlarged hard axillary nodes, the largest 1 cm in diameter Radical mastectomy was done and the tumor proved to be a well differentiated Grade I carcinoma, largely intraductal There were several involved axillary nodes She was well for 21 3 years following operation Then she began to have retrosternal pain and a hacking cough Roentgenograms showed metastases in the right pulmonary parenchyma and pleural fluid Thoracoscopy was done and firm yellow nodules were seen on the lung surface One of these was biopsied and proved to be a carcinoma, microscopically identical with the breast carcinoma removed many years previously She died without any other evidence of distant metastasis two years after her first pulmonary symptom

It might be said, in summary, regarding late local recurrence and metastasis of breast carcinoma, that the phenomenon is exceedingly rare after ten years It is so rare that it should not shake our confidence in our ability to cure the disease definitively with properly performed radical mastectomy When it does occur it is seen in well differentiated carcinomas of lesser malignancy which may be expected to progress slowly This fact suggests that it is the innate nature of the carcinoma, and not an increased resistance on the part of the host, that determines late recurrence

Edema of the Arm

The complications of shock and infection which were formerly to some degree, a hazard of radical mastectomy have been solved and edema of the arm is the only postoperative complication of any consequence It remains however the greatest penalty that women have to face after the average standard American radical mastectomy It is necessary first of all to define what we mean by edema. A good many patients following radical mastectomy have transitory slight increase in the diameter of the arm This might be defined as an increase of less than 3 cm in the diameter of the arm This amount of edema usually shortly disappears with the restoration of arm function An exception must be made for the baggy enlargement of the ventral aspect of the highest part of the upper arm This is seen in obese patients with relaxed tissues and results from severing the axillary fascia It cannot be avoided The edema to which I refer as a formidable complication affects the whole of the arm or the entire upper arm This kind of edema, which makes the patient socially unpresentable and which gives her a feeling of tension in the tissues of the arm might be defined as an increase in the diameter of the arm by more than 3 cm Holman and his associates found that one third of their patients had moderate edema of this kind The edema may become very severe and crippling, as in the patient shown in Figure 374 She was obese and was given postoperative irradiation to the axillary and supraclavicular regions Eleven per cent of Holman s patients had severe edema Daland found that 22.5 per cent of the patients at Pondville had moderate or severe edema

In tabulating the frequency of arm edema, the patients in whom edema develops as the result of local recurrence of the carcinoma in the axillary and supraclavicular regions should be set apart, or excluded This type of edema is not directly related to the surgery that has been performed What might be called *surgical* edema, that developing in patients who have been treated surgically but remain free of clinical evidence of axillary or supraclavicular recurrence should be further classified into two types. *Postoperative* surgical edema is the type that occurs immediately following operation It must be regarded as the consequence of some sort of fault in surgical technique *Secondary* surgical edema is the type that develops many months or years after operation as the result of a new infection in the arm through a portal of entry on the hand or arm The surgeon can not be held responsible for secondary edema, except to the extent that he may have failed to warn his patient that any minor wound or infection on the hand or arm subsequent to radical mastectomy is a serious matter

It is sometimes difficult to distinguish true postoperative edema from the edema developing as a result of later infection For instance, the patient may go home after operation and shortly thereafter burn her forearm while cooking, with the result that she develops edema for which her surgeon is truly not responsible.

As I see patients in consultation whose operations have been performed in a great variety of hospitals I am impressed by the frequency of edema of the arm. It is present, I would guess, in moderate or severe degree in between one third and one half of the patients whom I see

In my own series of patients for whom I have been personally responsible for

the wound healing there have fortunately been very few who have developed *postoperative* edema In the series of 356 patients which I have referred to above, 4 8 per cent developed postoperative edema of moderate degree (an increase of 3 cm or more in the diameter of the arm), and none developed severe postoperative edema The incidence of *secondary* edema has been greater After intervals of from ten months to nine years following operation, 7 6 per cent of my patients developed moderate edema, and two others developed severe edema In almost



Fig 374 Severe edema of the arm developing in an obese patient who was given postoperative radiotherapy to the axillary and supraclavicular areas

all of those who have developed secondary edema I have been able to identify the portal of entry of the infection

I believe that one of the reasons why I have had so little postoperative edema in my patients is that I have always dressed my wounds myself Even in the ward patients for whom I acted as a first assistant while my resident surgeon operated, I have done the postoperative dressings with the resident, supervising every detail until I felt certain that the resident had a sound knowledge of how to care for these complex wounds

Halsted, with his wonderful facility for discovering the essential truth of every problem that he put his mind to, was the first to describe the clinical picture of

edema of the arm following mastectomy He called it elephantiasis chirurgica He correctly described the two types which I have mentioned—that which follows shortly after operation and that which may develop any time subsequent to operation sometimes years later following an episode of infection I quote his description of the former type A few months ago I interviewed a patient who each year for sixteen years following an operation by me at the Johns Hopkins Hospital for cancer of the breast has had one or two and occasionally three or four attacks of redness and swelling of the arm on the operated side. The first symptoms malaise and nausea were quickly followed in the severe attacks by a chill and fever and then by slight redness and increased swelling of the arm The arm of this patient was observed to be swollen a few days after operation

Halsted also correctly interpreted the cause of postoperative edema as infection due to bad wound healing He said Now it is within the experience of every surgeon, especially of those who employ plastic methods to cover the defect, that frequently marginal necroses of the flaps occur and occasionally sloughings of considerable dimensions and it is usually in these cases that the swelling of the arm is most pronounced Attendant upon the necrosis there is infection and inflammatory reaction in varying degree and the greater the reaction the greater in general the swelling of the arm immediate and ultimate Halsted found that when the axillary flap was not sutured under tension and axillary dead space was avoided swollen arms of dimensions sufficient to distress or annoy the patient were no longer observed marginal necroses rarely occurred and the grafts took throughout with few exceptions we have been led to conclude that swelling of the arm follows the plastic operations [that is bringing the flaps together without grafting] in greater proportion and in more pronounced form than is seen in the cases treated by skin grafting

There has been a good deal of recent investigation of the cause of edema of the arm using modern methods of studying pathological physiology These modern studies support Halsted s original observation to the effect that edema is due to infection occurring in the arm with an impaired lymphatic circulation

From studies of the axillary vein by venography some years ago Veal came to the conclusion that obstruction of the vein is the important factor in postoperative arm edema Others using this same method of study have been unable to find any permanent obstruction of the vein in patients with edema. There is now enough evidence available to justify the conclusion that arm edema is not due to obstruction of the axillary vein

I have myself long been convinced that infection is the underlying cause of edema of the arm I learned this by seeing edema follow bad wound healing resulting from brutal surgery and improperly supervised postoperative wound care It seemed to me that the problem of edema needed concentrated study by a surgeon expert in the problems of surgical infection as well as those of carcinoma of the breast I persuaded my associate David Habif eminently qualified in both of these disciplines to undertake a concentrated investigation of edema of the arm He has, I am convinced, made important advances in the understanding of the pathological physiology of the phenomenon as well as in its treatment. Most of what follows has been derived from his work

To understand edema of the arm it is necessary to think in terms of our modern

knowledge of the physiology of the lymphatics We know that the blood carries water, electrolytes, and proteins toward the periphery of the body The water and the electrolytes are freely diffusible from the capillaries into the extracellular spaces Some water and electrolytes are absorbed by the lymphatics, while the remainder diffuse back into the venules Some protein leaks from the capillaries and is also absorbed by the lymphatics

The superficial subdermal lymphatics probably have only a minor role in the drainage of fluid from a limb The main drainage is through the lymphatic trunks situated in the deep subcutaneous tissue, and the deep lymphatic trunks in the deep fascia and underlying muscles When radical mastectomy is performed, these main lymphatic trunks of the subcutaneous tissue and the deep fascia are severed through a radius of at least 180° around the ventral aspect of the arm The main lymphatic trunks from the arm drain into the axillary lymph nodes, and these are, of course, almost all extirpated As a result, lymphatic drainage from the arm must be carried on through alternative routes These are probably the lymphatics over the cephalad and dorsal aspects of the shoulder and those of the posterolateral chest wall In assessing the degree of interference with lymphatic function in the arm following radical mastectomy and in edematous arms, we have relied upon an ingenious and very useful *lymphatic function test* devised by Dr David Ju and recently described by him The test is performed as follows Three cc of saline solution and 2 cc of the patient's serum are added to 25 microcuries of radioactive iodinated albumin Five cc of this solution is then injected into the dorsal aspect of the web-space between the 1st and 2nd digits Background counts of radioactivity are taken, using the contralateral arm With a specially shielded Geiger counter with a long window the edematous arm is studied in three sections—hand, forearm, and upper arm Counts are taken immediately after injection and after forty-eight hours Approximately 75 per cent of the injected dose is absorbed within a forty-eight hour period in a normal arm In contrast, during the first two weeks following radical mastectomy the percentage of injected material absorbed is much lower, the average being about 45 per cent absorbed in forty-eight hours After from two to four weeks the percentage absorbed increases almost to a normal level, so that the reading is approximately 65 per cent at the end of forty-eight hours These facts indicate that following the sudden extirpation of the major portion of the lymph nodes into which the arm lymphatics empty, collateral circulation usually develops within one month It is significant that the percentage of material absorbed following radical mastectomy never reaches normal, indicating that the lymphatic reserve is markedly encroached upon In most patients, however, no edema results Edema, then, must be due to some other factor that causes a further encroachment upon the lymphatic drainage of the arm The evidence indicates that this is *infection*

Studies in the operating room show that there is a considerable contamination of the air with hemolytic Staphylococcus aureus, coagulase positive In addition, a high percentage of the personnel in the operating room, including the medical and nursing staff, are carriers of the same pathogenic organism Routine cultures of radical mastectomy wounds prior to closure in our hospital show that approximately 28 per cent are contaminated with hemolytic Staphylococcus aureus The

contamination is probably either from the air in the operating room or is sprayed from the noses and throats of the operating room personnel rather than from the skin of the patient The contamination in a radical mastectomy wound may thus be introduced at the very outset

Perfect healing of radical mastectomy wounds is apt to be achieved only by the very expert Other surgeons often have a varying degree of necrosis of the skin flaps because they handle them too roughly or suture them too tightly Cultures of necrotic skin are almost always positive for hemolytic Staphylococcus aureus Another common source of infection is the dead space in an imperfectly obliterated axilla Serum and blood accumulating in this dead space provide a perfect culture medium for the growth of the organisms often present in the wound The infection may be of such slight degree as to escape the attention of the surgeon entirely It is sufficient however to obstruct lymphatic flow beyond the critical level and fluid begins to accumulate in the arm

We have demonstrated over and over again that when arm edema develops, early treatment with the proper antibiotics given within a period of one to five or seven days after its onset, will result in a normal arm When the infection is promptly checked the edema gradually disappears It is important to point out that the hemolytic Staphylococcus aureus commonly cultured in hospitals is often resistant to penicillin and to Terramycin or tetracycline. Cultures should be taken from mastectomy wounds that are infected and the proper antibiotic selected on the basis of sensitivity tests It is important to elevate the arm during the time the antibiotic is given If no organism is recovered the patient should be treated empirically It has been found that in our hospital the hemolytic Staphylococcus aureus is most often sensitive to bacitracin erythromycin and chloramphenicol If there is not marked improvement within a period of three to five days another antibiotic should be tried When an organism is found that is sensitive to penicillin or streptomycin or tetracycline they also may be employed. Therapy is continued for a minimum period of seven to ten days If the wound is open the antibiotic treatment should be continued longer If there is necrosis of the skin flaps the necrotic tissue should be excised, in order to obtain a clean granulating wound as soon as possible The wound may be treated locally with an antibiotic Neomycin and bacitracin have been the most useful locally

Just how infection interferes with the lymphatic outflow and produces edema is not clear It seems likely that the infection travels down into the lymphatics of the arm itself involving the smaller lymphatic plexuses both in the subdermal region and in the deep subcutaneous region of the arm We do not know the mechanism by which these lymphatics are obstructed or their absorptive function diminished Mucopolysaccharides or possibly chondroitin sulfate may be deposited in them They may be blocked by the deposition of fibrin The fact remains that if the infection is treated early the process is reversible In most instances when the infection is treated late and edema has been present for some time treatment with antibiotics is usually not successful In such cases it is likely that a degree of fibrosis has become well established and has blocked lymphatics extensively

A large proportion of patients receiving intensive radiotherapy following radical mastectomy develop lymphedema If the edema was present prior to

radiotherapy it is often accentuated The radiodermatitis with moist desquamation of the skin which results from intensive irradiation provides an ideal portal of entry for infection In an arm in which the lymphatic circulation is already critical, edema is to be expected following irradiation One of the advantages of supervoltage therapy, as compared with 250 kilovolt therapy, is that the skin may be spared and moist desquamation avoided Daland, Lobb and Harkins, and Holman and his associates, all found irradiation to be an important factor in the causation of arm edema

The patient who escapes edema of the arm immediately following radical mastectomy should be told by her surgeon that she is vulnerable to this complication for the rest of her life She must be made to realize that any trauma to the hand or arm which provides a portal of entry for bacteria may lead to infection and edema Burns, cuts and abrasions, and paronychia, are the most frequent sources of infection Patients should be urged to avoid manicurists because manicurists invariably push the cuticle back and in this way induce a minor degree of infection Although a good many patients have such minor local infections without developing cellulitis of the arm, they should all be warned to be alert for the slightest sign of the development of more extensive infection This should be reported at once to the responsible surgeon and treated with a suitable antibiotic If a positive culture can be obtained from the source of the infection and the sensitivity of the organism determined, the choice of antibiotic is easy If the antibiotic has to be chosen empirically it is important to keep in mind that unless there is prompt regression of the signs of arm infection within a period of three or four days it should be assumed that the organism is not sensitive to the antibiotic that is being given Another should be tried

Acute superficial cellulitis developing in an arm after radical mastectomy has been called erysipeloid The name is a good one The patient develops pain, swelling, and redness, usually involving a considerable area of the upper arm and sometimes the chest wall She feels acutely ill with chills and a temperature which may reach 104° or 105° F Figure 375 shows the zone of redness over the upper arm, the shoulder, and the skin flaps on the chest wall in a patient of mine whose infection developed from a paronychia of her right finger which is shown in Figure 376 Her radical mastectomy had been done five months previously and she had had no preceding edema of the arm She was admitted to the hospital after two days of shaking chills and malaise Her temperature was 105° F p r. on admission She was given sulfadiazine and her infection subsided within forty-eight hours She did not develop any subsequent edema of the arm and is well today, 10 years later

A patient with this erysipeloid syndrome is best treated by being admitted to the hospital and put to bed with her arm elevated while the correct antibiotic is administered This kind of hospital care is important if subsequent permanent edema of the arm is to be avoided

Before the development of antibiotics these patients who had developed the erysipeloid syndrome faced a dread future Although the acute infection would subside spontaneously after a few days, the organisms apparently persisted in the tissues of the arm because at intervals of every few months the syndrome would recur without any obvious new portal of entry for organisms With each

Fig. 375 Acute erysipeloid cellulitis of the arm shoulder and chest wall, developing as a result of a paronychia

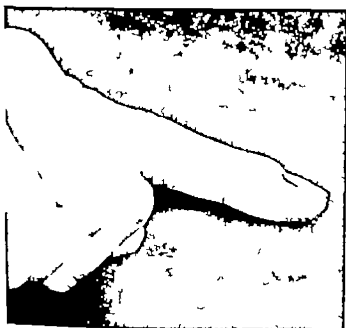


Fig. 376 The paronychia which was the portal of entry for the infection in the patient shown in Figure 375

new bout of infection the edema of the arm would increase Ultimately a marked degree of brawny edema would result In this kind of edema the tissues of the arm are tense and firm, and the patient has a constant feeling of tension in the arm It is an exceedingly uncomfortable and crippling condition

For the patient with well established chronic edema of the arm which has been present for some time, antibiotic treatment alone is comparatively ineffectual. In the past a number of surgical methods have been devised for treating edema of this kind In 1912 Kondoleon proposed sleeve resection of the subcutaneous tissues and deep fascia of the arm with the aim of providing new lymphatic channels between the superficial and deep lymphatics Although a good many of these Kondoleon operations have been done, the results have been so poor that the method has been generally abandoned More recently, Hutchins has proposed transplantation of the latissimus muscle across the axilla during radical mastectomy, in the hope of providing better lymphatic drainage and avoiding subsequent edema Guthrie has treated edema by inserting celloidin strips into the subcutaneous tissues of the arm, and Treves has used laminated gelfoam rolls in a similar way Standard treated edema of the arm by suturing the edematous arm to the lateral chest wall I cannot believe that any of these methods have any practical value because they do not attack the underlying basic problem in edema of the arm, namely, the abolition of the underlying infection

Perhaps the most important factor which limits our ability to abolish infection in a chronically edematous arm is obesity Obese patients must reduce drastically if they are to hope to have much improvement in the condition of the arm The arm rarely returns to a normal size, however If the patient is having recurrent attacks of cellulitis, antibiotic therapy should be thoroughly tried This should be done in the hospital with the arm elevated, using either intermuscular bacitracin, oral erythromycin, or oral chloromycetin Bacitracin is given intramuscularly in doses of 20,000 units every eight hours over a period of seven days, taking care to observe the precautions necessary with bacitracin Erythromycin is given orally in doses of 200 milligrams every six to eight hours Chloromycetin is administered orally in doses of 500 to 750 milligrams every eight hours

For those patients who have lost weight and in whom the infection is controlled or abolished yet the edema persists, it is worth while to try hyaluronidase injections Hyaluronidase is an enzyme with the specific action of depolymerizing hyaluronic acid Its entire mechanism of action is, however, not known If the edema is of sufficient degree and hardness, and has been present over a long period of time with marked fibrosis of the subcutaneous tissues, it is probable that hyaluronidase will not be effective However, it is worth trying Habif administers it as follows The patient is hospitalized Two 50 cc syringes, each containing 50 cc of saline and 150 turbidity reducing units of the enzyme (Wydase) are employed After applying antiseptic solution to the arm, the hyaluronidase solution is injected through a number 24 gauge, three-quarter inch, hypodermic needle, directly through the skin and layered on the deep subcutaneous stratum above the deep fascia From 5 to 10 cc of the solution is instilled at points 5 cm apart throughout the area of edema Two sterile Zobec 5-yard rolls are then applied to the hand, forearm and arm up to the axilla Two 4-inch elastic bandages are then used to give moderate compression of the entire arm.

The arm is elevated for a period of three hours The bandages are then removed and the patient is allowed up as desired No further elevation is carried out until the following day when the treatment is repeated It is usually given daily for a period of five days. The patient is discharged from the hospital to return in a period of from one to two months If the treatment is effective and infection does not recur it will be noted that after the first one to two courses of treatment the arm softens and subsequently begins to shrink

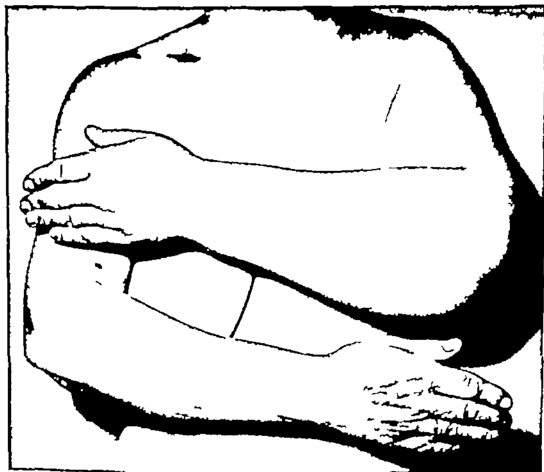


Fig. 377 Marked edema of the left arm following radical mastectomy with a wound infection.

Habif has found that in patients treated with hyaluronidase in whom the infection has been abolished or controlled, the method has been successful in reducing the arm to almost normal size In patients in whom the infection persists, although of low-grade, there has been a moderate degree of improvement of the edema. In both of these groups of patients weight reduction is essential if they are obese Figure 377 shows an obese patient with a marked degree of edema of the left arm which developed following radical mastectomy with a wound infection The improvement of her arm after a year s treatment with hyaluronidase and a considerable reduction in her weight is shown in Figure 378

It must be emphasized that there is another group of patients in whom the infection persists in the arm despite the most vigorous use of antibiotics Habif has found that in these patients his hyaluronidase treatment is of no benefit

The hyaluronidase treatment as Habif gives it, requires an extraordinary

new bout of infection the edema of the arm would increase Ultimately a marked degree of brawny edema would result In this kind of edema the tissues of the arm are tense and firm, and the patient has a constant feeling of tension in the arm It is an exceedingly uncomfortable and crippling condition

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Table 151 Relative Results of Radical Mastectomy from Various Hospitals

Period covered by study	Author and date of pub	Hospital	No primary cases with rad mast	Percentage with invol. axil. nodes	5-yr cl cure rate	5-yr surv rate	10-yr rate
19[illegible]4–1933	Eggers et al. 1941	N Y Skin & Cancer Hosp	253	63 7	33 5		21 7 Cure
1916–1941	McGraw 1947	Henry Ford Hospital	41	50 9		43 0	
1936–1940	Taylor 1949	Massachusetts Gen Hosp	395	59	52		
1936–1941	Nohrman 1949	Radiumhemmet Stockholm	767	61 7		50 6	[illegible]9 2 Surv
1931–1944	Nielsen 1951	Radium Centre Copenhagen	544	49		56	33 Surv
1935–1940	Lewison et al. 1953	Johns Hopkins Hospital	204	61 8	38 7	44 1	
1930–1939	Williams et al. 1953	St. Bartholomew's Hosp London	338	not given		42 9	26 0 Surv
1924–1943	Boyd et al. 1954	Univ of Penna. Hospital	417	61 8 of those reviewed	35 3	42 8	
1936–1947	Bryant et al 1954	Univ of Michigan Hosp	440	55	50 7	58 4	
1935–1942	Haagensen and Stout 1948	Presbyterian Hospital	495	61 6	49 7	59 3	38 0 Cure 4 4 Surv
1910–1944	Harrington 1952	Mayo Clinic	7445	57 8		50 4	
1930–1945	Finney et al 1947	Private Cases 4 Surgeons Union Mem H	298	43 9 of traced patients	50 4	54 0	
1929–1945	Trout 1950	Jefferson Hosp Roanoke, V Private cases	219	55 of traced patients	52	54 3	
1935–1950	Haagensen Personal Series Ward and Private	Presbyterian Hospital, N Y	356	55 1	56 7	66 6	44 Cure 49 5 Surv

These relative survival and clinical cure rates represent the number of survivors as well as the number of recurrence-free patients expressed as percentage of all primary cases in which radical mastectomy was performed during the stated period of years. In some cases this meant a recalculation of published rates which were based on traced cases only. Reports that did not include complete data were omitted.

These data show the results achieved with the surgical attack under four different types of clinical organization

The data from the Radiumhemmet and the Copenhagen Radium Centre represent what has been achieved with radical mastectomy supplemented with irradiation in special cancer hospitals

The data from the University of Pennsylvania Hospital, the Johns Hopkins Hospital and St. Bartholomew's Hospital show the results obtained with radical mastectomy in large general hospitals, where there was no specialization the operations being done by all members of the surgical staff

The results reported from certain large American general hospitals like the

degree of perseverance by him as well as by the patient Yet I am convinced from seeing what he has achieved with it that it is very much worth while, and that it represents an important advance in therapy

Meanwhile edema of the arm remains a common and crippling complication of mastectomy It can be avoided only by a meticulous surgical technique which achieves perfect wound healing I believe that one of the important factors in achieving perfect wound healing is skin grafting of the operative wound, because, as Halsted pointed out so long ago, it avoids the triad of tension on the skin flaps, necrosis, and infection



Fig 378 Improvement in the arm edema of the patient shown in Figure 377 after hyaluronidase treatment and weight reduction

Comparative Results of Radical Mastectomy in Various Clinics

In summarizing what has been achieved with the surgical attack upon breast carcinoma, it is interesting to compare the recent results of radical mastectomy in various hospitals and private clinics throughout the world These are shown in Table 151 These are *relative* survival and clinical cure rates representing the number of survivors as well as the number of recurrence-free patients expressed as a percentage of all primary cases in which radical mastectomy was performed during the stated period of years In some cases this meant a recalculation of published rates which were based on traced cases only Reports that did not include complete data have been omitted It is regrettable that we have been unable to find more reports of the results of radical mastectomy meeting these strict minimal statistical standards

ness of modern surgeons that their results with cancer of the breast have been poor unfortunately has not led them to choose their patients more critically and to perform the operation more carefully It has discouraged some surgeons to the point of abandoning the surgical attack altogether, and handing their patients over to the radiotherapeutists Other surgeons have given up radical mastectomy for other operations Some of these have been less thorough and others more comprehensive than the conventional radical mastectomy The achievements of these various currently popular methods of surgical attack other than radical mastectomy must be viewed critically from three points of view First, what is their rationale? Second what is their morbidity and mortality? Third what is their curative achievement?

Simple Mastectomy There is a school of modern surgeons exemplified by Deaton Case Hartmann and Fitzwilliams, who believe that simple surgery gives just as good results as radical mastectomy By simple surgery is meant local removal of the tumor with a margin of surrounding breast tissue or simple removal of the breast The axilla is not dissected because the surgeon does not believe that breast carcinoma is curable by surgery when the axillary nodes are involved This philosophy of course goes back to Paget s time, and if these modern defeatists depended solely upon their surgical effort their results would be no better than Paget s But patients treated today by simple surgery usually receive both irradiation and hormonal treatment in addition with the result that life is prolonged and the therapeutic achievement, when expressed statistically is not much worse than the results of those surgeons who use radical mastectomy indiscriminately and unskillfully

From the patient s point of view the price she pays in mutilation and in morbidity is not appreciably greater for radical mastectomy than for simple mastectomy The mortality of both operations should be nil If she indeed has no axillary metastasis nothing of course is gained by dissecting the axilla, but if she happens to have axillary involvement of comparatively limited extent, the choice between simple mastectomy and radical mastectomy is often the choice between life and death. If her axillary metastases are not excised, the only defense against them is irradiation and it has been shown repeatedly that irradiation does not destroy carcinoma in lymph nodes with any certainty In contrast I have shown that radical mastectomy not supplemented by irradiation in my hands has given a 65 per cent five year clinical cure rate and a 74 6 per cent five year survival rate in patients with axillary metastases of limited extent The surgeon who is aware of these facts and who nevertheless chooses to rely upon simple mastectomy or upon simple mastectomy plus irradiation is not offering his patient her best chance of cure

Williams at St. Bartholomew s and McWhirter at the Royal Infirmary have advocated the latter treatment Neither of these able students of breast carcinoma could demonstrate an advantage in radical mastectomy as performed in their respective hospitals in terms of survival at five and ten years They therefore abandoned the operation Williams and McWhirter s data regarding the comparative results of radical mastectomy and simple mastectomy supplemented with irradiation, in their own hospitals must, of course be accepted What I object to is general condemnation of radical mastectomy

Massachusetts General Hospital and our Presbyterian Hospital, where there happens to have been special emphasis upon the study of breast carcinoma, and where much of the operating was done by a small group of surgeons particularly interested in the disease, seem to indicate that this degree of specialization is worth while It is of interest that reliance was almost entirely upon radical mastectomy in both of these hospitals, supplementary irradiation being used only to a very limited degree

Finally, the table presents the results of a number of surgeons operating upon private patients—the surgeons at the Mayo Clinic, four of those at the Union Memorial Hospital, and Trout at the Jefferson Hospital These results are similar to those achieved by a concentrated surgical attack in the Massachusetts General Hospital and the Presbyterian Hospital

Any comparison of these results of radical mastectomy in these various clinics is of limited value because of differences in the stage of the disease, as well as the criteria followed in selecting the patients for radical mastectomy Both of these factors are difficult to define on paper The extent of the variation in the stage of the disease is illustrated by an incidence of only 43 9 per cent of axillary metastasis in the private cases at the Union Memorial Hospital and an incidence of 63 7 per cent in the patients at the New York Skin and Cancer Hospital The criteria of operability also vary greatly in different clinics At the Massachusetts General Hospital and the Presbyterian Hospital, where similar criteria of operability have been used, patients have been selected more strictly than in several of the other hospitals

The data as a whole, however, give a general impression of what can be achieved today with the surgical attack on the wards of teaching hospitals, and in private clinics

I have added my own personal results, which include both ward and private cases, because I wish to emphasize again that it is possible to achieve still higher cure and survival rates by more rigorous selection of patients for operation I have no illusion that my operative technique is much of a factor in achieving these results But they certainly represent my ambition to refuse operation to all patients whom I cannot cure I have recently been learning, with my regional lymph node biopsies, to sort out additional patients whose carcinoma is beyond the reach of the Halsted radical mastectomy When I report my results with these recent patients in another decade, I hope to have considerably higher cure and survival rates The advantage, as I have already pointed out, of this kind of very strict selection is not only that it avoids futile and harmful operations, but that it makes it possible to achieve results with which other methods of treatment will have to compete This kind of competition will I hope lead us toward the truth If radiotherapy cannot, for example, achieve as high survival and cure rates as the Halsted mastectomy has achieved, even when the cases to be irradiated are chosen with the same strict criteria, then we will know that the operative attack is truly preferable Until such comparable results are available we can only guess what is the best method of treatment

Operations Other than the Halsted Radical Mastectomy

When radical mastectomy is used indiscriminately for cancer of the breast, and when it is performed indifferently, its results are poor The growing aware-

Extended Operation Including Excision of Internal Mammary and Supraclavicular Lymph Nodes None of the operations which I have discussed above, including the Halsted mastectomy attempts to remove any but the axillary lymph nodes They are therefore all inadequate in terms of our modern knowledge of the occurrence of metastases in other regional lymph node groups —the internal mammary and the supraclavicular nodes In an attempt to meet this challenge, a variety of new operations have recently been devised which combine some type of mastectomy and axillary dissection with removal of either the internal mammary or the supraclavicular nodes or both These extended operations present a new and very difficult kind of technical challenge to surgeons In a general way it may be said that mammary carcinoma can be successfully attacked surgically in regions in which the anatomy permits adequate surgical exposure, and when the foci of disease are far enough away from vital and irremovable structures so that the dissection can be done gently and at a distance of at least several centimeters from the actual carcinoma These conditions are fulfilled for example when metastases exist in only a few lymph nodes situated in the middle axillary region That is why axillary metastases of this kind can be removed with comparative success But when the surgeon attempts to excise cancerous lymph nodes lying immediately upon the pleura as in the internal mammary region or nodes lying upon the confluence of the internal jugular and subclavian veins deep behind the clavicle, and he has to carry his dissection within a few millimeters of the carcinoma, the likelihood of success seems small In attempting to remove internal mammary metastases there are special difficulties at the level of the first interspace This interspace is usually so narrow that ligation of the internal mammary vessels and section of the second costal cartilage at the sternal edge brings the dissection into actual contact with the metastases. The disease is not only incompletely removed but it is often implanted widely in the operative field A fact which adds to difficulty of successful surgical excision of internal mammary metastases is that the metastases may not be conveniently localized in lymph nodes They are often found permeating lymphatics and blood vessels, or infiltrating the areolar tissue of the internal mammary region The line of resection cannot be carried far enough away from these foci of carcinoma because of anatomical limitations

The pertinent question regarding the new operative attack upon internal mammary and supraclavicular metastases is not whether it is safe this has been well established It can also be said that although most of these extended operations add somewhat to the disfigurement of the patient as compared with a well performed Halsted mastectomy this added penalty to the patient would be a small price for an increased chance of cure The important question is whether these extended operations can get out metastases from these surgically difficult regions and really add to the number of cures This question cannot be answered yet. The new operations have been done for so short a time that no long term end results are available.

The likelihood of an over all improvement in the success of the surgical attack upon breast carcinoma with the use of these extended operations is to some degree dependent upon another factor This is the fact that the surgical closure of the chest wall defect left by the internal mammary excision necessitates some

because it has failed in certain hospitals, where it may have been performed indiscriminately without any selection of patients, and with indifferent techniques My own experience has convinced me that, in patients selected according to strict criteria, meticulous radical mastectomy achieves results superior to those of any combination of limited surgery and irradiation

Simple mastectomy has frequently been used as a palliative procedure to rid the patient whose carcinoma was clearly inoperable, of an ulcerated tumor As the efficacy of radiotherapy in controlling the primary tumor has improved, the need for such palliative simple mastectomy has decreased I have personally abandoned simple mastectomy for this purpose because I have found that radiotherapy does better

Another use of simple mastectomy which I must strongly condemn is its use by surgeons who find themselves in a diagnostic dilemma and compromise by performing partial or simple mastectomy, with the intention of proceeding with a radical mastectomy when a definitive microscopical diagnosis becomes available In so doing they are very apt to sacrifice their patient's only chance of cure because the initial partial dissection cuts across actual carcinoma and implants it widely Lockhart and Ackerman reviewed a series of cases where simple mastectomy had been done preceding radical mastectomy and found the results disastrous

Mastectomy Plus Axillary Dissection. A compromise between simple mastectomy and radical mastectomy consists in the removal of the breast and an axillary dissection, leaving the pectoral muscles intact C C Holman has recently made a plea for this type of conservative operation Any surgeon who has attempted to dissect the axilla without excising or cutting across the pectoral muscles knows that only the lower axillary nodes can be removed by this method I have shown, in Chapter 19, that the most frequent site of metastasis, even when only a few nodes are involved, is in the middle scapular and central groups of nodes

Patey, at the Middlesex Hospital, has also preserved the pectoralis major muscle in his surgical attack upon breast carcinoma, on the assumption that it is not invaded except in very advanced cases He states that he has not seen recurrence in the muscle when it was thus preserved He gains access to the axilla by lifting the patient's arm so that it points toward the ceiling, and by retracting the pectoralis major medially, preserving its nerve supply The pectoralis minor is cut across close to its attachment to the carocoid process In this way Patey states that he is able to dissect out the contents of the axilla in the usual way up to the lateral border of the first rib

When the pectoralis major muscle is preserved, and remains to form a bridge across the axilla, the patient is, of course, less disfigured than after the Halsted mastectomy

The vital question of whether or not this type of compromise operation achieves as low a local recurrence rate and as high a clinical cure rate as the Halsted mastectomy cannot be answered today because truly comparable end result data are not available Until such proof of the adequacy of this limited surgical attack is provided I prefer to depend upon the Halsted operation

Lymph Node Chain Margottini and Bucalossi were the first to make internal mammary dissection a routine part of their radical mastectomy and in 1949 were able to report 110 such operations performed in Milan and in Rome. They resected about 2 cm of the second and third costal cartilages and then ligated the internal mammary vessels above in the first interspace and below in the third interspace, and removed the vessels and accompanying lymphatics and nodes and fat extrapleurally

3 Radical Mastectomy plus Supraclavicular Dissection plus Extrapleural Excision of the Internal Mammary Lymph Node Chain Dahl Iversen and his associates in Copenhagen began in 1948 to dissect the supraclavicular nodes as part of their radical mastectomy In 1950 they extended their surgical attack to the internal mammary nodes They evolved a conservative method of removing them extrapleurally by cutting the second third and fourth costal cartilages 1 to 1 5 cm from the sternal border The costal cartilages were then raised with gauze strips so that the internal mammary vessels and nodes were exposed The vessels and all accompanying lymphatic and fatty tissue were removed in this way from the upper four interspaces

Not enough time has as yet elapsed to give us any indication of the end results of this comprehensive surgical attack which the Danes have undertaken They have demonstrated that their conservative extrapleural method of excising the internal mammary nodes is not mutilating or dangerous, but they have not yet shown that it increases the cure rate

In France, Redon has devised a surgical attack similar to the Danish method in that it combines radical mastectomy with extrapleural excision of the internal mammary chain and supraclavicular dissection It is more mutilating than the Danish method in that the supraclavicular dissection is combined in the same operative field with the radical mastectomy and internal mammary dissection by cutting the clavicle Such an operation will certainly have more morbidity and mortality than the Danish operation In a series of 100 cases Redon found internal mammary metastases in 22 per cent.

4 Radical Mastectomy Combined with en bloc Resection of the Chest Wall in the Internal Mammary Area More radical surgical methods of combining radical mastectomy with en bloc resection of the full thickness of the chest wall in the internal mammary area have been devised by Urban and by Ariel in New York In the Urban operation a comparatively large area of chest wall in the internal mammary region is removed The sternum is split, and the second third fourth and fifth ribs cut just lateral to their costochondral junctions. This leaves a defect of considerable size in the chest wall which Urban closes with a fascia lata graft Urban reports one operative death in 160 such operations In 40 per cent of his cases neither axillary nor internal mammary metastases were found The internal mammary nodes alone were involved in 6 per cent of the cases The axillary nodes only were involved in 24 per cent. Both internal mammary and axillary nodes were involved in 30 per cent. Thus, in 64 per cent of the patients in whom Urban resected the chest wall to remove the internal mammary nodes, no metastases were found in them

Ariel's operation attempts to achieve resection of the internal mammary lymphatics by a more conservative excision of the full thickness of the chest wall

limitation of the thoroughness of the removal of the breast and the other tissues on the chest wall. In our clinic we believe that the thoroughness of the chest wall part of our Halsted mastectomy has a definite curative value. I hesitate to sacrifice this advantage for the questionable gain from internal mammary dissection.

These are some of the reasons why I have stated my criteria of operability in Chapter 26 in terms of the conventional Halsted mastectomy, which continues to be our main reliance. Most of the patients in whom we have proved the presence of internal mammary metastases with our biopsy technique are treated with irradiation.

It is nevertheless our duty to cautiously explore the possible value of the extended surgical attack upon these regional lymph node metastases. But I have stated elsewhere, and I reaffirm it here, that experience has taught me that *when carcinoma has involved the lymph nodes at the apex of the axilla, the supraclavicular nodes, or the internal mammary nodes in the first interspace, no conceiveable form of surgical attack will succeed.*

There remains the possibility of surgical excision of metastases in the internal mammary nodes in the lower interspaces. We are keenly interested in this challenge and have performed resections of the internal mammary area in occasional cases in which it seemed likely on clinical grounds that metastases might exist in the lower interspaces, and in which we had proved by preliminary biopsy that there were none at the apex of the axilla or in the first interspace. We have found very few cases of this type, and our experience with the extended surgical attack is therefore so limited that we must depend upon the experience from other clinics, where the criteria used to select cases for internal mammary dissection are less strict. I shall review the various types of extended operative attack upon regional lymph node metastases which are currently being tried out.

1. Mastectomy plus Axillary Dissection plus Extrapleural Excision of the Internal Mammary Lymph Node Chain. Richard Handley, to whom we owe the original proof of the importance of internal mammary metastases, has recently described a new operation which includes extrapleural resection of the internal mammary chain from the first to the fifth interspace. He first biopsies the internal mammary lymph node in the first interspace. If it is found not to be involved he proceeds with the first part of his operation which consists of dissection of thin skin flaps as in radical mastectomy. The breast, together with the pectoral fascia, is then dissected off from the pectoralis major muscle, which is preserved. The axilla is then dissected by lifting the patient's arm toward the ceiling and retracting the pectoralis major medially, and severing the pectoralis minor, according to the technique devised by Patey. The internal mammary chain is excised as a separate and final step. A block of the chest wall, including the second, third, and fourth costal cartilages, the intervening intercostal muscles, and the underlying internal mammary vascular bundle, is removed extrapleurally. Handley closes the defect in the chest wall with the pectoralis major muscle, which he has preserved for this purpose.

Handley and Patey report having performed a total of 57 of these operations. The internal mammary nodes were found to be involved in 40 per cent of the cases.

2. Radical Mastectomy plus Extrapleural Excision of the Internal Mammary

Ten years later the patient is perfectly well The bony defect on her chest wall does not trouble her

A Summary of the Surgical Attack upon Carcinoma of the Breast

A study of the comprehensive absolute results of the treatment of carcinoma of the breast, which in America has been predominantly surgical reveals that only between 30 and 40 per cent of all primary carcinoma patients survive five years The relative five year survival rate for radical mastectomy that is, the number of patients surviving among those who were operated upon has been approximately 50 per cent The five year clinical cure rate that is the percentage of patients who continue free of recurrence five years after operation is about 10 per cent less

These comparatively poor results of radical mastectomy have discouraged surgeons and led them to perform the operation indifferently Critical analysis indicates that the results of radical mastectomy are poor because the operation is done indiscriminately on most patients who come with the disease in a large proportion of whom it is inoperable At Columbia we have evolved clinical and biopsy criteria of operability which have enabled us to prove that in about 50 per cent of patients who come with breast carcinoma today the disease is beyond the reach of the conventional radical mastectomy and should not be operated upon. When such criteria of operability are followed, and a meticulous and thorough radical mastectomy of the Halsted type is performed, highly satisfactory results are achieved even in patients who have axillary metastasis of limited extent, in whom the disease is otherwise operable I have personally achieved a five year survival rate of about 75 per cent in these patients with axillary metastases of limited extent No other method of treatment gives such good results They justify the continued reliance upon the operation and encourage a meticulous performance of it

Less *aggressive as well as more radical methods of surgical attack, are being* currently tested. Simple mastectomy should be unqualifiedly condemned because it fails to attack the axilla in curable patients with a limited degree of axillary involvement. At the other extreme the unreasonably radical operations such as those of Wangensteen and Prudente are unjustified because they have a high penalty for the patient without offering her any increased chance of cure

The most reasonable modifications of radical mastectomy are those which include excision of the internal mammary lymphatic route Some of these procedures particularly those of Dahl Iversen and Handley do not penalize the patient appreciably

The gain from removal of these nodes is doubtful because we know that they are often involved at a comparatively advanced stage of carcinoma of the breast, a stage at which all methods of treatment are likely to fail to cure. The carcinoma has begun to escape through lymphatics in all directions in the form of minute emboli like a river in flood overflowing its banks Stemming the flow in one direction will not block the flood

No end results are yet available for the extended radical mastectomy It is upon this evidence that the value of the new operations will have to stand or fall While this evidence is being collected their indiscriminate use should be condemned for more harm than good will surely result if they are widely

Ariel sacrifices only about 2 cm of the second, third and fourth costal cartilages, together with the underlying chest wall He is able to close a narrow defect of this kind with steel wire sutures through the costal cartilages

Radical Mastectomy Combined with Supraclavicular Dissection and Internal Mammary and Mediastinal Lymph Node Dissection. Wangensteen and Lewis, at the University of Minnesota, have been performing a considerably more radical surgical attack upon breast carcinoma It includes not only the conventional radical mastectomy but a supraclavicular dissection as well as a dissection of the internal mammary and mediastinal lymph nodes To achieve this the chest is opened widely by splitting the sternum and detaching the first rib and elevating the clavicle The operation has recently been done in two stages Lewis reports a 13 per cent operative mortality in a series of 50 patients In something over 40 per cent of the patients no lymph node metastases were found in any of the dissected areas

I cannot conceive of any justification for this operation It has a high morbidity, a considerable mortality In a high percentage of the patients in whom it was done it was unnecessary, and I suspect that in the others it has been futile

Mastectomy Combined with Interscapular-thoracic Amputation. The ultimate in surgical attack upon carcinoma of the breast, namely, mastectomy combined with interscapular-thoracic amputation, has been advocated for advanced cases by Prudente, and by Jerram and Langmead In his series of 12 patients Prudente reports 2 cured for eleven and seven years, respectively, but neither of these had supraclavicular metastasis, one of the chief indications Prudente gives for his operation

Radical Mastectomy Combined with Resection of the Full Thickness of the Underlying Chest Wall. There are rare cases in which resection of the full thickness of the chest wall may be a lifesaving procedure We have one such case in the records at Presbyterian Hospital The details of her history follow

Mrs F F, aged 52, came to me in May, 1946, with the story that three years previously she had noticed a small dimple in the middle of the inframammary fold of the left breast She went to her family physician who told her it was "only scar tissue and of no importance " When I saw her first, three years later, she had a 4 × 3 cm hard tumor lying in the nipple line of the inframammary fold of the left breast Over the center of the tumor there was a crusted cleft in the skin The tumor lay over the fourth interspace and was solidly fixed to the underlying chest wall In the course of its growth the carcinoma had pulled the breast inward toward the inframammary fold, turning the nipple downward and inward, elevating and generally contracting the lower half of the breast The resultant deformity of the breast was very great There was, however, no edema of the skin There were no enlarged axillary or supraclavicular nodes Skeletal and chest films were negative

A radical mastectomy, combined with resection of the full thickness of the chest wall, underlying the carcinoma, was performed by Drs Humphreys, Stevenson and myself Portions of the fourth, fifth and sixth ribs and costal cartilages were included The resection was done in one piece The pleural surface of the resected chest wall was grossly normal The comparatively large defect in the chest wall was covered with a sleeve of skin and subcutaneous tissue cut from the abdomen and shifted upward Study of the operative specimen showed that the carcinoma had involved the overlying skin as well as the underlying pectoralis muscle The intercostal muscles were not involved Twenty-nine axillary lymph nodes were identified and two of these were found to contain metastases

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One of the first such studies was that carried out by Lenz in our own clinic in the Presbyterian Hospital. Between 1933 and 1937 a total of 38 patients with breast carcinoma, most of them with comparatively advanced disease, were treated intensively with roentgen rays. The breast and the axilla each received a tumor dose of up to 4500 r during a total period of six to eight weeks. At most 2000 r measured in air was administered to each of superior, inferior, mesial and lateral breast fields. The roentgen beams were placed tangential to the chest wall. After a varying interval of time radical mastectomy was performed. The surgical specimens were meticulously studied by Stout. The microscopical changes in some of these cases were described by Beach. They illustrate the

Table 152. Microscopical Effects of Roentgen Therapy

Year	Author	No. of cases treated	Tumor dosage	Persisting ca. in breast		Persisting ca. in axillary nodes
				No.	Per cent	Number
1947	Lenz	38	up to 4500 r	38	100	31 of 38
1950	Lumb	60	2000 to 4500 r	53	88.4	not reported
1951	Williams	36	3000 to 3500 r	35	97.1	14 of 24
1953	Peters	135	4000 r	111	82	not reported
1955	Baclesse	77	4500 to 9500 r	68	88.1	51 of 72

effects of irradiation on mammary carcinoma cells very well. The earliest change is perhaps suppression of mitosis. The nuclei then become pyknotic, the cytoplasms vacuolated. Abnormal cell division occurs with the formation of bizarre and gigantic cells. Changes of this kind are shown in Figure 379. The tumor cells finally disintegrate and disappear. Meanwhile, fibrosis of the stroma develops and the remaining carcinoma cells are imprisoned in dense collagen. Figure 380 shows residual carcinoma cells in a dense fibrous stroma of this kind. Figure 381 shows a biopsy of the same carcinoma before irradiation. The radiation effect may be so marked that only scattered individual carcinoma cells can be identified, as in Figure 382. Ultimately calcification may develop in the areas of fibrosis as shown in Figure 383. Despite these marked microscopical effects of radiation seen in Lenz's series of cases, Stout was able to find persisting carcinoma cells in every case, although in some cases only a very few remaining cells could be identified, and they were so distorted that their viability might be questioned.

The microscopical effects of irradiation which I have described have been those produced in the primary breast carcinoma. It was our experience that the changes in the axillary lymph nodes produced by equivalent doses were not as marked. Figure 384 shows axillary metastasis after intensive fractionated irradiation had been delivered to it. It has been the experience of most workers that

CHAPTER 28

THE RADIOTHERAPY OF BREAST CARCINOMA

The irradiation treatment of carcinoma of the breast is a subject of great importance, because, as I have indicated in Chapter 26, about half of the patients who come to us are not operated upon but are sent to the radiotherapeutist In a treatise such as the present one I cannot attempt as a surgeon to present the technical details of radiotherapy These must be sought for in books on radiotherapy I wish, however, to present certain basic facts and principles concerning the use of irradiation in breast carcinoma

Irradiation is used in carcinoma of the breast in three ways (1) as a primary method of treatment attempting to cure the disease, (2) as an auxiliary form of therapy supplementing radical mastectomy, again with the intention of cure, (3) as a palliative method of therapy These three usages are best discussed separately They all depend, however, upon the same biologic effect of irradiation upon mammary carcinoma, and it is helpful to consider this fundamental matter before discussing the special usages of irradiation

The Biological Effects of Irradiation upon Mammary Carcinoma

Although we do not know the precise mechanism by which irradiation damages cells, we know from clinical and microscopical observations that its effects are profound Tumor masses shrink and disappear The carcinoma cells themselves show marked morphological changes and finally disintegrate and disappear The degree of cell destruction depends not only upon the amount of irradiation reaching them but upon the relative sensitivity of the tumor cells to irradiation in comparison with the cells of the surrounding tissues Irradiation of sufficient intensity can destroy any tissue, but from a practical aspect the aim of the radiotherapeutist has to be to deliver a sufficient dosage to the carcinoma to destroy it without irreparably damaging the surrounding normal tissues

It is important to review the microscopical evidence as to what success has been achieved in the effort to destroy breast carcinoma The studies that are pertinent are all necessarily recent, because it is only recently that sufficiently fractionated irradiation, capable of delivering a high dosage to the carcinoma, has been employed To be of value such studies must include not only accurate data as to the dosage of irradiation delivered to the tumor, but after the completion of irradiation the breast and axillary contents must have been removed and detailed microscopical studies carried out Recent studies providing information of this kind are summarized in Table 152

Fig. 380 Atypical residual mammary carcinoma cells in a dense fibrous stroma

Fig 381 Pre-irradiation biopsy of mammary carcinoma shown in Figure 380

metastases in the lymph nodes are more resistant to irradiation than the primary tumor

Lumb studied the microscopical changes in a series of 60 cases of carcinoma of the breast treated by radiation at the Westminster Hospital, London In his cases the tumor dose ranged from 2000 to 4000 r , administered during a period of between 20 and 40 days Lumb found no remaining carcinoma in seven of the 60 cases Four of these were among the 11 cases in which a dose of 3500 to 4000 r had been given In the other seven cases in this group only small numbers of isolated cells showing gross degenerative changes were found The changes pro-

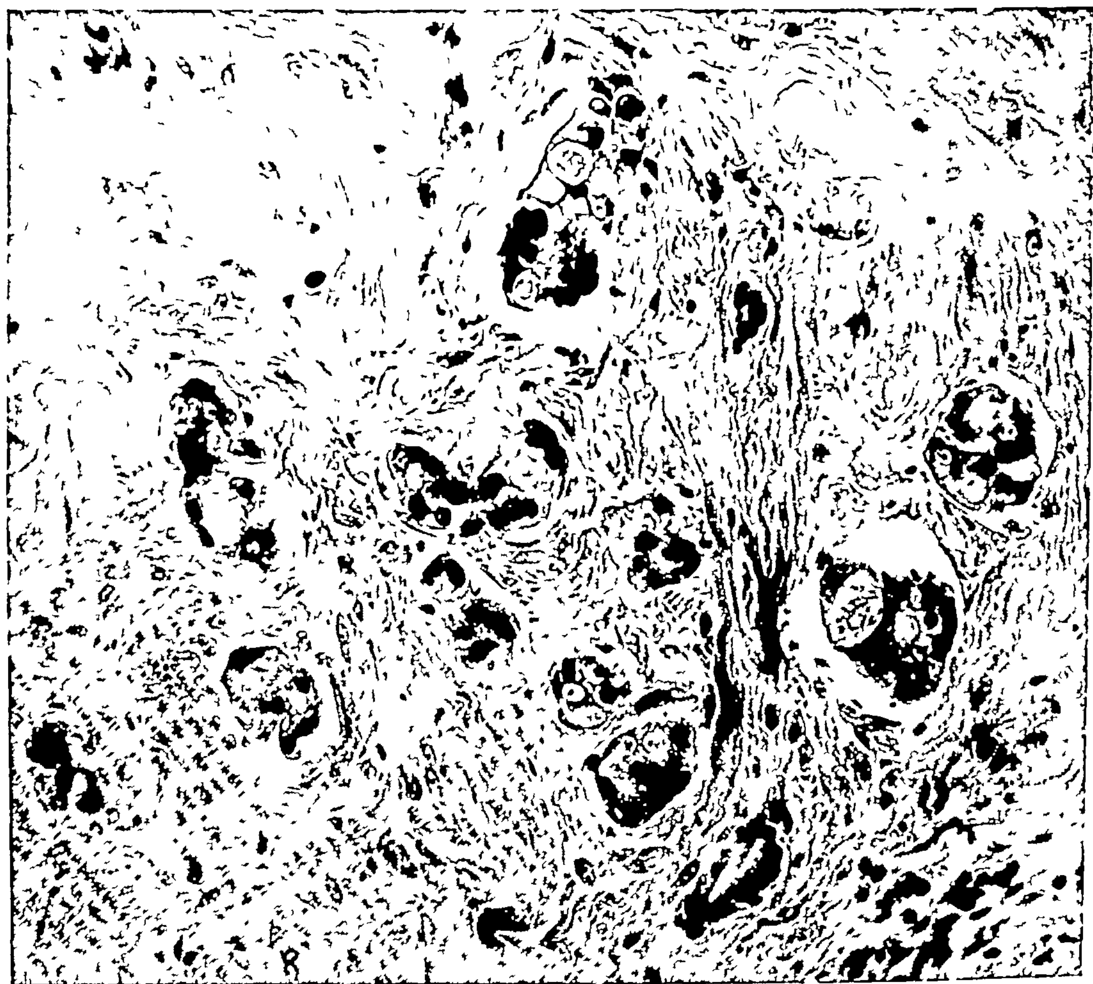


Fig 379 Pyknotic nuclei and vacuolated cytoplasm of irradiated mammary carcinoma cells

duced by dosages of 2500 r or less were slight Lumb concluded that a dose of between 3500 and 4000 r is required to destroy the majority of breast carcinomas

Williams described his findings in 36 cases treated by fractionated x-rays In 32 cases the dosage varied from 3000 to 3500 r , delivered in from 21 to 28 days In four other cases, the only ones which have been reported treated by supervoltage x-rays, the dose was 4500 r delivered in 30 days Williams' supervoltage was given with a 1000 kilovolt unit, using a half layer value of 9 2 mm of copper Residual carcinoma was found in the breast of 35 of the 36 cases The only case in which the tumor had been completely destroyed was one of the four treated

by supervoltage x rays In the 24 cases in which the axillary lymph nodes were removed and studied microscopically viable carcinoma was found in 14

Peters reported the microscopical findings in 135 cases in which a tumor dose of 4000 r was administered over a period of two weeks and radical mastectomy subsequently performed Residual carcinoma was found in 111 or 82 per cent of the cases Peters did not state how many lymph nodes were found to contain residual tumor

Baclesse is probably the foremost student of irradiation in the treatment of breast carcinoma He has recently reported his findings in a series of 77 patients



Fig. 384 The well preserved appearance of metastasis from a mammary carcinoma to an axillary lymph node after treatment with 4500 r

treated with x rays between the years 1935 and 1946 with subsequent radical mastectomy No Stage I cases were included The approximate tumor dose varied between 4500 and 9500 r At least two months, and sometimes much longer were required to deliver this amount of radiation. In 9 of the 77 cases no residual carcinoma was found in the breast In 51 of 72 cases microscopical study showed persisting carcinoma in the axillary lymph nodes

The apparent conclusion from these facts about the microscopical evidence of irradiation effect upon mammary carcinoma is that a tumor dose of at least 4500 r is required to produce marked morphological changes, and that even with the highest dosages yet employed, carcinoma persists in about four fifths of the cases. The carcinoma cells are locked up in a dense fibrous stroma but they are apparently viable. The threat that they may break free and begin to grow again

Fig 382 Isolated atypical mammary carcinoma cells persisting in dense fibrotic stroma after irradiation

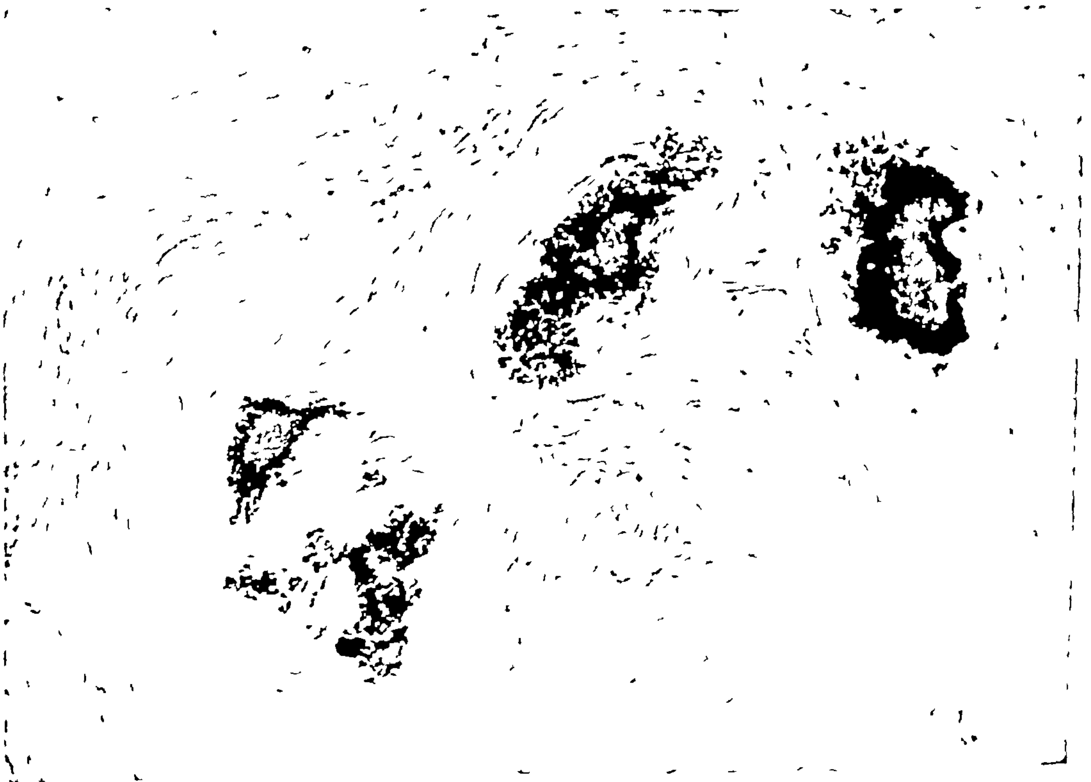


Fig. 383 Calcification in heavily irradiated breast tissue

again in 2 of these remaining patients In one (Mrs G P) it was the primary breast lesion that recurred and in the other (Mrs M McG) it was an axillary mestastasis Five of the patients remained alive at the end of fifteen years 2 with recurrent carcinoma One of these two has since died

Baclesse, in his last publication on the subject in 1952, reported his results in 130 patients treated with roentgen therapy during the years 1936 to 1945 The disease was comparatively advanced in all of these patients no Stage I cases being included For example, 94 of the patients had clinically involved axillary nodes and 10 had clinically involved supraclavicular nodes The dosages ranged from 4100 r to 9500 r Baclesse usually took 16 to 18 weeks to administer these large doses In 41 of these 130 patients the primary tumor disappeared and had not recurred after five years The relationship between the dosage delivered to the tumor and Baclesse's results is so interesting that I have reproduced the table in which he presented his data (Table 154)

Table 154. Results of Roentgen Therapy in Breast Carcinoma
(after Baclesse 1952)

Tumor dose r	Cases treated stage II, III	Tumor disappeared for a minimum of 5 yrs.
4100	4	2
4500–5000	14	0
6000–6500	30	11
7000–8000	29	10
9000–9500	18	9
9500	17	6
Total	112	38

Baclesse is the only radiotherapeutist relying upon irradiation alone for the control of breast cancer who has reported in detail the morbidity of the method I have reproduced his table (Table 155) listing the complications following radiotherapy in 156 patients whom he treated The local telangiectasia which he lists as the most frequent complication is not a serious one, although unsightly Baclesse's patients developed edema of the arm less often than ours, perhaps because he gave his treatment so slowly that he avoided the more marked exudative skin reactions which we have often seen Edema of the arm following irradiation may become extreme and may be a great cross for the patient to bear

The most serious disadvantage of the radiotherapeutic attack upon carcinoma of the breast is the tendency of the disease to recur locally long after an initial satisfactory regression I have personally seen a number of cases in which local recurrence developed more than five years after the initial treatment, and I feel that we must reserve judgment concerning the permanence of arrest obtained with irradiation until more data are available concerning long term follow up of patients treated in this manner The following case illustrates such a late recurrence of the primary tumor

remains one of the basic disadvantages of irradiation treatment Finally, it would appear that mammary carcinoma is just as difficult, if not more difficult, to destroy when it is growing as metastasis in lymph nodes as in its primary focus in the breast

Primary Treatment with Roentgen Therapy

Reliance upon roentgen rays as a primary method of treating carcinoma of the breast, even when it is in the so-called operable stage, is a comparatively recent development which has been carried on only in a few centers The use of

Table 153. Primary Irradiation Treatment of Breast Carcinoma

Year reported	Author	Hospital	No of cases	Years of treatment	Tumor dosage	5-yr survival		10-yr survival	
						No	Per cent	No	Per cent
1952	Lenz	Presbyterian Hospital	46	1938 to 1940	4000 to 6900 r	10	21 5	7	15 2
1952	Baclesse	Curie Institute	130	1936 to 1945	4100 to 9500 r	41	31 2		
1955	McWhirter	Royal Infirmary Edinburgh	1882	1941 to 1947	3750 r	786	42	122 of 480	25

x-rays for this purpose has evolved with the modern development of fractionated intensive treatment which has made it possible to deliver sufficiently large tumor doses to profoundly affect breast carcinoma This type of primary radiological treatment has evolved chiefly under Baclesse at the Curie Institute in Paris McWhirter at Edinburgh has popularized it Lenz in our own clinic treated a small series of patients exclusively with x-rays fifteen years ago, and the distant results in his series are now available The data from these three clinics is shown in Table 153

Lenz's series of patients treated primarily with radiation included 46 patients treated during the years 1938, 1939 and 1940 These were all patients who had been judged unsuitable for radical mastectomy because of the local and regional extent of the disease Fifteen patients were given a tumor dose of less than 5000 r The primary tumor persisted in all of these Thirty-two of the patients were given doses of 5000 to 6900 r to the breast These doses were administered over a period of between two and three months In 24 of the 32 patients with the higher tumor dosage the primary tumor disappeared Ten of the 46 patients were still alive five years after treatment, but in one of them the disease had recurred after three years and was progressing In the interval between five and ten years the carcinoma began to grow again locally in 2 more, after five and one-half and six years, respectively At the end of ten years 7 of the original 46 patients remained alive In the interval between ten and fifteen years the carcinoma began to grow

current carcinoma in the axillary region slowly increased in size. Her arm became edematous and began to pain her a good deal Figure 385 shows the area of axillary recurrence Figure 386 shows her edematous arm, and the telangiectatic crusted skin over the breast. Even though the patient s disease has finally begun to progress again it must not be forgotten that irradiation held it in check for more than 14 years, and that it was originally too advanced to attack surgically



Fig. 385 Reactivation of carcinoma in axillary lymph node 14-1/2 years after irradiation treatment.

McWhirter of course has treated the largest number of patients with irradiation by far His technique is rather different from that of Baclesse in that his tumor dose is only 3750 r and it is given over a period of only three weeks McWhirter has achieved a 42 per cent five year survival rate and a 25 per cent ten year survival rate with his method of treatment. I have classified McWhirter s method of treatment as primarily radiotherapeutic although in the majority of his cases a partial mastectomy is performed. I use the term *partial* mastectomy rather than *simple* mastectomy because the operation that is carried out in McWhirter s patients certainly does not remove the entire breast In an anatomical sense it is a partial mastectomy The removal of the bulk of the breast that is carried out greatly reduces the mass of tissue which McWhirter must treat and makes his task easier from the point of view of the physics of irradiation

Mrs G P , aged 48, came to Presbyterian Hospital in February, 1939, with a tumor of the right breast which she said she had had for three weeks She had a 10 cm carcinoma filling the central area of the right breast There was edema of the skin over the central portion of the breast There was a clinically involved node in the right axilla

It was decided that the carcinoma was inoperable, although there was no evidence of distant metastasis, and she was treated with irradiation given through four fields to the breast and three fields to the axilla, each field receiving approximately 2000 r , over a period of three months The tumor dose to the breast lesion was 5600 r Both the primary tumor and the axillary metastasis disappeared The patient had no further evidence of her carcinoma until August, 1951, twelve years and three months after her radiation had been completed, when a number of small recurrent nodules were found in the skin along the lower portion of the right edge of the sternum These were treated successfully with radiation but during the following year new skin nodules continued to appear in the skin over the right chest Carcinoma finally appeared in the opposite breast and she developed bone metastasis

Table 155 Postradiotherapy Complications in 156 Patients Treated by Radiotherapy Only (after Baclesse 1952)

	No of patients	Per cent
Marked telangiectasis	30	20
Telangiectasis plus scleroses plus edema	26	17
Pectoral muscle sclerosis	14	9
Moderate edema of the arm	8	5
Pulmonary sclerosis	11	7
Skin necrosis	10	6
Neuritis	3	1 5
Pathological fracture of rib	1	0 6
Paralysis	1	0 6

The following case is one from our series in which the primary tumor in the breast remained under control, but the axillary metastasis began to grow after being held in check for many years

Mrs M McG , aged 52, came to the Presbyterian Hospital in February, 1940, with a tumor of the central portion of the left breast which she had had for seven months The tumor measured 5 cm in diameter It was freely movable over the chest wall There was a very small area of edema of the skin just caudad to the areola The nipple was markedly retracted There was a small satellite nodule in the skin just lateral to the areola In the lower left axilla there was a firm 1 cm node

There were no evidences of distant metastasis

It was decided that her carcinoma was locally inoperable and her breast was treated through four portals and the axilla through three portals Each of these received 2000 r excepting the superior and inferior breast portals which received 1500 r This treatment was given over a period of four months The breast tumor regressed, leaving only an area of thickening The axillary node also disappeared There was no reactivation of her breast disease until fourteen and a half years later, in November, 1954 On a follow-up examination on that date I noted that at the site of the original node in the lower axilla there was a recurrent tumor measuring 2 cm in diameter There was a small ulcer in the overlying skin The breast itself showed no change, although the skin showed marked telangiectasia and atrophy During the following year the area of re-

current carcinoma in the axillary region slowly increased in size Her arm became edematous and began to pain her a good deal. Figure 385 shows the area of axillary recurrence Figure 386 shows her edematous arm, and the telangiectatic crusted skin over the breast. Even though the patient s disease has finally begun to progress again it must not be forgotten that irradiation held it in check for more than 14 years, and that it was originally too advanced to attack surgically



Fig. 385 Reactivation of carcinoma in axillary lymph node 14-1/2 years after irradiation treatment.

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But this very limited operation cannot possibly be regarded as curative in the sense that it removes the entire carcinoma Simple mastectomy is done today in Edinburgh very much as it was done 75 years ago in German clinics, where Halsted himself found that it achieved an average *three year* cure rate of only 16 per cent McWhirter's superior results are certainly attributable to the irradiation which he gives all his patients That is why I have chosen to discuss his methods in the present chapter dealing with irradiation



Fig 386 Edema of the arm developing following reactivation of axillary metastasis 14-1/2 years after irradiation treatment

In terms of the penalty to the patient of primary irradiation treatment as compared with radical mastectomy, it should first be said that neither method of treatment need have any mortality There is no doubt whatever that the penalty in terms of morbidity of a badly done radical mastectomy, particularly if edema of the arm develops, is greater than for skillfully given irradiation But the comparative morbidity of the two methods must be discussed on the assumption that both forms of treatment are administered with an equal degree of skill Baclesse has documented the morbid complications of irradiation in his series of cases McWhirter has not attempted to describe them I can readily forgive him this omission because the penalty to the patient is difficult to define Irradiation dam-

age to the lung, although less frequent since tangential rather than direct irradiation of the chest wall has been in use still remains an appreciable hazard as Baclesse s data indicate The atrophic telangiectatic skin over an irradiated breast is more vulnerable to damage than a thick skin graft and I believe that the likelihood of edema of the arm is as great following intensive radiation as following radical mastectomy The irradiated patient however retains her breast scarred

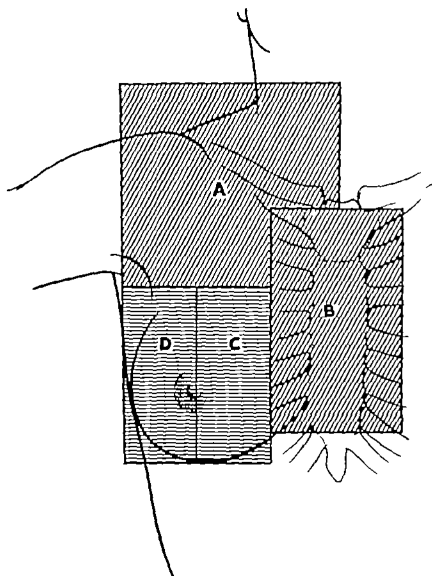


Fig. 387 Portals used for primary treatment of breast carcinoma with 2000 kilovolt x-rays.

and indurated though it may be, and this is undoubtedly from her point of view a great psychic advantage. Ackerman has recently attempted an evaluation of McWhirter's method

The one solid fact that stands out in a critical comparison of radical mastectomy and primary roentgen irradiation is that neither McWhirter Baclesse, nor any of the leading radiotherapeutists who have attempted this form of therapy have presented data to indicate that they can achieve a five or ten year survival rate with irradiation, no matter how their cases are selected for treatment, which

can approach the results achieved in the Presbyterian Hospital and elsewhere with the Halsted radical mastectomy performed on cases strictly selected according to our criteria of operability

At the Francis Delafield Hospital the strict application of our clinical and biopsy criteria of operability to breast carcinoma during the last four years has resulted in our classifying a comparatively large number of patients with the disease as inoperable Those so classified have all had to be treated by irradiation In many there were no demonstrable distant metastases, and the primary car-

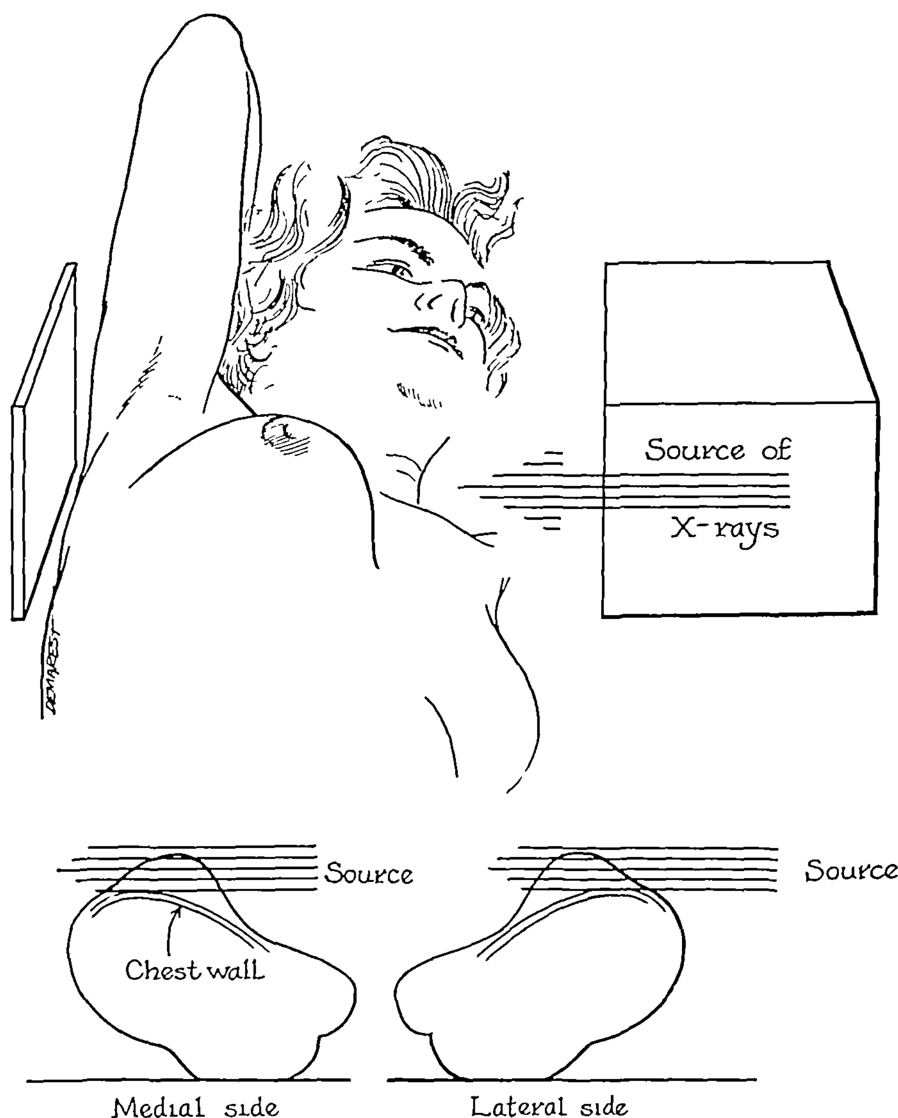


Fig 388 Tangential irradiation to the breast through two fields, with 2000 kilovolt x-rays

cinoma was small The feature that made them inoperable was the presence of occult metastases in the internal mammary, apex of axilla, or supraclavicular lymph nodes Dr Maurice Lenz, our radiotherapeutist, and his successor, Dr Ruth Guttmann, have evolved a method of treatment, using 2000 kilovoltage, which seems to have certain advantages

The physical factors used are a half value layer of 7 mm of lead and a target skin distance of 100 cm

The irradiation is given through four portals as indicated in Figure 387 The two breast fields each measure 15 x 15 cm and are directed tangentially as shown in Figure 388 The internal mammary field in the average patient measures 15 x 8 cm The field covering the axilla and supra and infraclavicular regions averages 12 x 16 cm All four portals are given a tumor dose of 200 r daily over a period of five weeks or more The total tumor dose administered to each of the four fields varies between 5000 and 6000 r

Patients usually tolerate this irradiation very well The skin reaction which develops occurs somewhat later than with the conventional 250 kilovolt type of

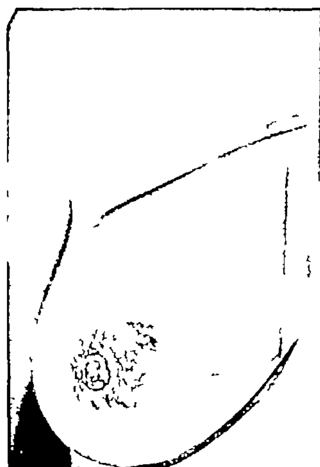


Fig. 389 The mild skin reaction produced over the breast with intensive irradiation with 2000 kilovolts.

irradiation, and is much less marked In most patients only a mild tanning develops as shown in Figure 389 Moist desquamation is usually avoided. This mild skin reaction contrasts sharply with the severe reaction which followed the conventional 250 kilovolt irradiation formerly used and which delivered a considerably smaller tumor dose Figure 390 shows a patient with the severe reaction produced by 250 kilovolt treatment.

As late as three years following completion of the treatment the patients have not shown any severe fibrotic or telangiectatic change

Patients treated with the 2000 kilovolts have less malaise and nausea Their blood picture must of course be followed with the customary care necessary when high doses of irradiation are given

can approach the results achieved in the Presbyterian Hospital and elsewhere with the Halsted radical mastectomy performed on cases strictly selected according to our criteria of operability

At the Francis Delafield Hospital the strict application of our clinical and biopsy criteria of operability to breast carcinoma during the last four years has resulted in our classifying a comparatively large number of patients with the disease as inoperable Those so classified have all had to be treated by irradiation In many there were no demonstrable distant metastases, and the primary car-

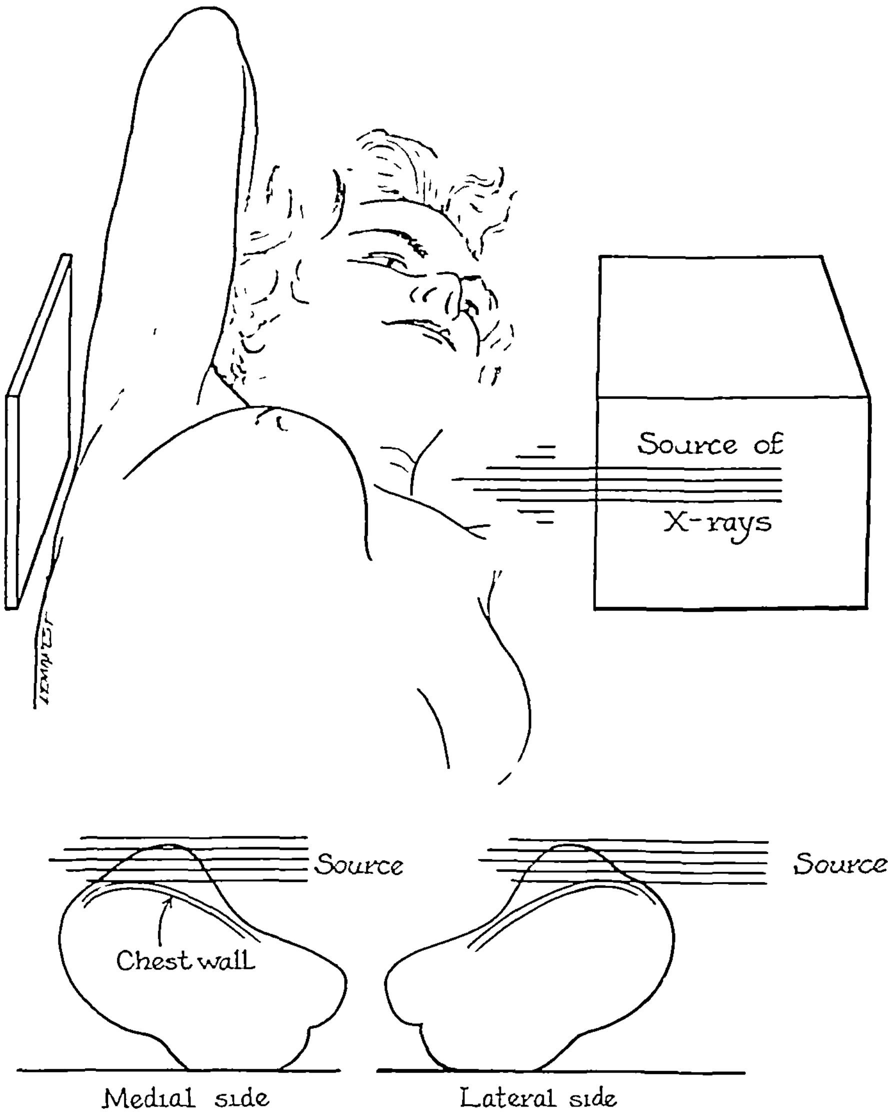


Fig 388 Tangential irradiation to the breast through two fields, with 2000 kilovolt x-rays

cinoma was small The feature that made them inoperable was the presence of occult metastases in the internal mammary, apex of axilla, or supraclavicular lymph nodes Dr Maurice Lenz, our radiotherapeutist, and his successor, Dr Ruth Guttmann, have evolved a method of treatment, using 2000 kilovoltage, which seems to have certain advantages

The physical factors used are a half value layer of 7 mm of lead and a target skin distance of 100 cm

the irradiation and microscopical studies carried out on the surgical specimens In a series of 77 cases studied in this manner Ross reported that carcinoma persisted in the breast of 42. Persisting carcinoma was found in the axillary lymph nodes in 14 of 50 cases It is clear from this evidence that interstitial radium does not succeed any better than roentgen rays in destroying carcinoma completely in the breast

McKittrick took up the method and in 1937 reported his results with it in 96 patients treated at the Palmer Memorial Hospital He concluded that interstitial radium is inferior to surgery as a method of treating primary operable carcinoma of the breast, (1) because of its late after effects which include pain along the free margin of the pectoral muscle, accompanied by a palpable thickening in this region and partial limitation of abduction of the arm and (2) because of the microscopical persistence of the disease in surgical and autopsy specimens McKittrick s experience has discouraged others in this country from using interstitial radium for breast carcinoma. Even at St. Bartholomew's Hospital where the method originated, interstitial radium has been replaced by x rays in combination with simple surgery

Radiation Supplementing Radical Mastectomy

A generation ago it was the general practice to supplement radical mastectomy with radiation given either pre- or postoperatively Postoperative radiation was the most popular and it was usually given in small doses repeated at intervals of weeks or months on the basis of the theory that this kind of treatment would restrain the growth of residual carcinoma Critical evaluation of the results of radical mastectomy supplemented by this kind of radiation by such able students of the disease as Harrington (1935) and Greenough (1929) failed to show any advantage of this combined treatment over radical mastectomy alone When Dr Stout and I published our study of end results at the Presbyterian Hospital for the period of 1915 to 1934 inclusive, we were likewise unable to demonstrate any advantage of either preoperative or postoperative irradiation German radiotherapeutists, such as Hintze, and Anschütz, were the chief proponents of supplementary prophylactic irradiation The method gradually fell into disfavor with the realization that the dosage delivered to the tissues by this kind of feeble interrupted irradiation was not sufficient to have much effect on carcinoma.

Thus it has come about that the results with breast carcinoma during recent years in such American clinics as the Massachusetts General Hospital, Mayo Clinic, and here at the Presbyterian Hospital have been achieved by radical mastectomy alone not supplemented by pre or postoperative irradiation.

In some European clinics however irradiation of the modern intensive fractionated type delivering a comparatively high tissue dosage, has been used to supplement radical mastectomy during recent years At the Radiumhemmet in Stockholm and at the Radium Center in Copenhagen preoperative radiation has been favored. Richards in Toronto has also advocated preoperative irradiation Berven Nielsen and Ash and his associates report from the three above mentioned clinics that preoperative radiation has given an improved survival rate in their cases with comparatively advanced disease Miller and Pendergrass studying their data at the Hospital of the University of Pennsylvania, were unable to

I have been reluctant to perform partial mastectomy upon these patients destined to be treated by irradiation, believing that any surgery may do harm. The great majority of them have therefore been treated exclusively by irradiation In a few, in whom the diseased breast was of massive proportions and Dr Lenz and Dr Guttmann felt that removal of its bulk was a necessity, this has been done

It is as yet too early to report any distant results of this method of primary irradiation of breast carcinoma It is clear that a higher tumor dose can be



Fig 390 Severe skin reaction with intensive irradiation with 250 kilovolts

delivered with it and that it penalizes the patient less than our previous 250 kilovoltage treatment Whether or not it will give a better survival rate remains to be seen

Primary Treatment with Radium

In 1922 Geoffrey Keynes began a unique experiment at St Bartholomew's Hospital, in which he treated breast carcinoma by inserting radium needles into the breast and regional lymph node areas By 1937 he had treated a total of 325 patients in this manner He was able to report that some 46 per cent had survived five years He believed that his method was superior to radical surgery, particularly in the more favorable group of patients In 1924, treatment with interstitial radium by Keynes' method was begun in a separate series of cases on the Surgical Professorial Unit at St Bartholomew's In this series of cases the breast and axillary contents were removed at intervals of from three to six months after

seemed likely on clinical grounds, or in patients in whom the existence of such metastases had been proved by biopsy We know that Halsted mastectomy can deal successfully with the disease on the chest wall and in the axilla in properly selected cases but we have as yet very little knowledge of the efficacy of radiation in controlling internal mammary and supraclavicular metastases In view of our modern knowledge of the frequency of metastases in these lymph node groups this question becomes one of great practical importance Our experience at the

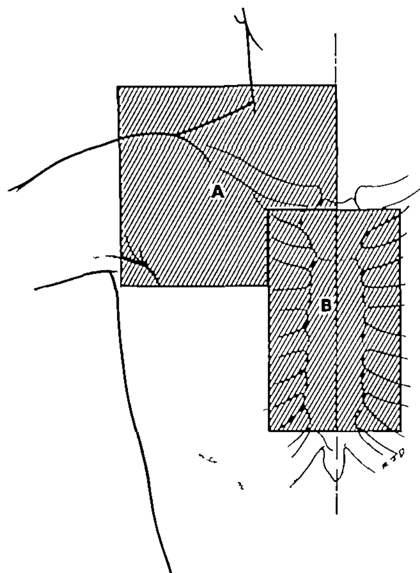


Fig. 391 Portals used for supplementary postoperative radiation to the internal mammary area and the axillary and supra and infraclavicular areas

Delafield Hospital where proved internal mammary and supraclavicular metastases have been irradiated with a tumor dose of 5000 r or more in many patients suggests that metastases in these internal mammary and supraclavicular regions are controlled by this kind of irradiation for as long as the patients survive Unfortunately almost all succumb with distant metastases within three years If further experience confirms this fact a therapeutic attack in which irradiation is used to complement Halsted mastectomy is not justified because mastectomy should not be done when cure cannot be hoped for

find any evidence that radiation, given either before or after operation, improved the end results

I have not reproduced any of the statistical data bearing on the question of the value of prophylactic pre- or postoperative radiation because my impression after studying it is that its interpretation is difficult and somewhat questionable The results depend so much upon the stage of the disease in the groups of patients whose treatment is being compared, and this is such a difficult matter to define, that no clear cut conclusions can be drawn

Our own attitude in regard to the use of preoperative supplementary radiation is as follows We regard approximately 5000 r as the minimal tumor dose likely to arrest breast carcinoma We cannot deliver this to the breast and regional lymph node areas in less than six weeks We dare not carry out the type of radical mastectomy which it is our custom to perform, with thin skin flaps and a skin graft, until the radiation reaction has regressed satisfactorily This takes a minimum of another month or two We therefore face the necessity of delaying our surgery at least four months or more if we give what we regard as adequate preoperative radiation We feel that this is too long a time to delay our definitive therapy

Postoperative irradiation of similar intensity cannot be given to our thin skin flaps and our skin grafts on the chest wall These tissues will not tolerate it It can, however, be given to the internal mammary, axillary, and supraclavicular areas In patients in whom there is extensive axillary involvement—and by this I mean that the majority of the axillary nodes dissected from the specimen are found to contain metastases—it has been our practice to give postoperative prophylactic irradiation As the accuracy of our criteria of operability has improved we have less often blundered into operating upon patients with extensive axillary disease, so that the occasions on which we have to give postoperative irradiation are not many When we have to give it Dr Guttmann prefers to employ 2000 kilovoltage She uses two portals, as shown in Figure 391 The internal mammary field averages 8 x 15 cm , and the field covering the axilla, and supra- and infraclavicular regions averages 12 x 16 cm Both fields are given a daily tumor dose of 200 r over a period of five weeks A total tumor dose of 5000 r is delivered to the internal mammary field as well as to the axillary, infra- and supraclavicular field The physical factors used are the same as for our 2000 kilovolt primary irradiation plan of treatment, and the skin reaction produced is similarly mild The penalty to the patient of this type of prophylactic irradiation is not great, and we hope that the irradiation adds to her chance of cure

Radiation Complementing Radical Mastectomy

If the view is taken that surgical excision of metastases in internal mammary and supraclavicular nodes has little chance of success and therefore should not be attempted—and that is in general my own opinion—the possibility of complementing operation by radiation may be considered The disease on the chest wall and in the axilla would be removed by Halsted mastectomy, and the internal mammary and supraclavicular metastases dealt with by radiation This complementary use of surgery and irradiation is technically feasible It might be utilized in patients in whom the existence of metastases in these lymph node groups

voltage, using 3 mm of aluminum as a filter with a target skin distance of 30 cm A field of sufficient size to surround the lesion with a generous margin is used A skin dose of 350 to 450 r is given at each treatment, a total of 3000 r being administered during a three week treatment period

It is in my opinion an error to excise skin nodules surgically Surgical excision is not only much less successful than irradiation but excision carries a risk of producing further embolism and metastasis of the carcinoma

One of the most valuable uses of irradiation is in the treatment of metastasis to bone Treatment should be begun at once when pain suggests the likelihood of



Fig. 393 Regression produced by a tumor dose of 5000 r (2000 kilovoltage) to the carcinoma shown in Figure 392.

bone metastases, even though they cannot be seen roentgenographically In this way the patient is spared unnecessary pain If the involvement of bone is generalized it is of course impossible from a practical point of view to use roentgen therapy but in most patients the bone metastases are few and isolated, at least at an earlier stage *in the metastatic process For such lesions no other therapy is* as successful as irradiation

For the treatment of bone metastases Dr Guttmann prefers to use 250 kilovoltage with a filter of 2 mm of copper and a target skin distance of 50 cm Deep-seated bone lesions are usually treated through opposing fields When this method cannot be employed oblique fields may be used to avoid a moist skin reaction A daily tumor dose of 200 r is given A total tumor dose of 2000 to 2500 r is delivered over a period of from two to three weeks

Approximately three-quarters of patients with bone metastasis who are treated

The Palliative Use of Roentgen Therapy

It was formerly my custom to do palliative simple mastectomy for fungating tumors which were so objectionable locally that something had to be done about them As the years have gone by and my appreciation of the ability of modern, intensive, fractionated roentgen therapy to produce regression of breast carcinoma has grown, I have come to abandon surgical palliation and rely entirely upon radiation for this purpose What can be achieved with irradiation in the local control of a fungating tumor is illustrated by the following case



Fig 392 Massive fungating, hemorrhaging carcinoma of the right breast

Mrs H D, age 45, came to the Delafield Hospital with a huge, fungating carcinoma, shown in Figure 392 Her husband had been ill for a long time and she had devoted herself entirely to his care, ignoring her breast tumor until a sharp hemorrhage from it brought her to us The massive carcinoma was solidly fixed to the underlying chest wall. Hemorrhage from a deep ulcerated area in its upper portion was arrested with electrocoagulation She was then treated with 2000 kilovoltage, 5000 r being administered to the tumor over a period of six weeks Three months later an additional 1500 r was given through a single small portal over the center of the lesion The tumor almost completely regressed, leaving only a small crusted area over its center The appearance of the patient six months after treatment was begun is shown in Figure 393

Roentgen therapy is much the preferred weapon in dealing with metastasis to the skin and local skin recurrence The fact that the skin nodules are small makes it possible to treat them through a very small field and to deliver to them comparatively large amounts of irradiation—so large that they are almost invariably controlled Dr Guttmann prefers to treat skin metastases with 100 or 120 kilo-

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with irradiation will get fairly satisfactory pain relief Table 156 shows the percentage of successful pain relief reported by several authors, and also the average survival time following the development of bone metastasis It will be seen that this was about one year Occasional patients will survive much longer following the successful treatment of bone metastasis, and live several years in comfort Nohrman reported that 33 3 per cent of the patients from the Radiumhemmet treated for bone metastasis lived more than one year, 15 8 per cent more than two years, 7 6 per cent more than three years, 5 3 per cent more than four years, 3 5 per cent more than five years, and 0 9 per cent more than eight years

More than 90 per cent of bone metastases are osteolytic in type Even when irradiation successfully relieves pain, it often fails to produce restoration of the

Table 156. Results of Roentgen Therapy of Bone Metastases from Cancer of the Breast
(after Garland, 1950)

Author	Number of cases	Percentage of pain relief	Average survival period (months after discovery of bone metastasis)
Lenz and Freid	31	71	11
Burch	41	70 6	15 5
Pohle and Benson	18	65	?
Copeland	74	?	18
Deucher	145	78	13
Leddy and Desjardins	106	80	?
Wulff	44	46	14 3
Bouchard	23	65	13 6
Garland et al	79	68 4	12

bony architecture Garland reported that this occurred in only 26 3 per cent of his cases treated with irradiation

Irradiation is much superior to hormonal treatment of bone metastasis It gives pain relief more quickly and more surely, and it does not have the unpleasant side effects of hormonal therapy

Irradiation is useful for pulmonary parenchymal metastases only if they are of limited extent and unilateral Bilateral metastases and pleural metastases should not be irradiated For patients whose pleural effusion accumulates so rapidly that they have to be tapped every few days the intrapleural administration of colloidal gold or nitrogen mustard is worth while It will produce a significant diminution in the effusion in at least 50 per cent of cases Gellhorn and Holland have described the technique of using colloidal gold When facilities are not available for handling radioactive isotopes nitrogen mustard may be used and gives similar results The method has been described by Karnofsky and his associates

Irradiation is of only temporary help in controlling metastases to the brain and spinal cord These types of metastases usually occur late in the course of the disease, and the patients are not likely to survive long Irradiation must be given very carefully when the intracranial pressure is elevated, because the edema resulting from it may produce a further rise in intracranial pressure

CHAPTER 29

THE HORMONAL TREATMENT OF MAMMARY CARCINOMA

The hormonal treatment for cancer of the breast is not only a recent development in the attack upon the disease but as of the present moment it must be regarded as a secondary form of treatment in comparison with surgery and radiation The former can be said to have a curative effect, but hormone treatment does not cure It has only a temporary restraining effect upon the course of the disease

Whatever I write today about hormonal treatment will necessarily be out of date tomorrow because of the rapid evolution of knowledge in this special field of investigation Treatment has so far been empirical and is based either upon the suppression of ovarian adrenal, or pituitary function by irradiation, upon removal of these glands or upon the administration of some one of the various estrogenic or androgenic hormones This therapy cannot in any way be regarded as scientific in the sense that it is dependent upon an understanding of the relationship of the origin and growth of mammary carcinoma to any of these hormones It has been suggested that certain mammary carcinomas are dependent upon estrogen for their growth but proof of this thesis is entirely lacking, because there are as yet no reliable quantitative methods for estrogen assay Although the disappearance of estrogen from the urine frequently coincides with improvement of breast cancer patients relapse is not always accompanied by the reappearance of urinary estrogen A cause and-effect relationship between the progression of cancer and the amount of estrogen present has not therefore been proved

All that I shall attempt to do in the present chapter is to present a brief review of what has been achieved by these various hormonal methods of treatment and to state our plan for the hormonal treatment of carcinoma of the breast

The Administration of Hormones

Both androgen and estrogen have been used therapeutically for breast carcinoma for more than fifteen years, and in great numbers of patients. Their effects have been described in many individual reports, some of which I will subsequently refer to By far the most valuable source of information concerning the value of these hormones, however are the reports of the Council of Pharmacy and Chemistry of the American Medical Association A committee of the coun

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proved subjectively by the androgen Objective improvement in terms of recalcification of bone defects was observed in from 10 to 20 per cent

As an example of the effect of androgen upon bone metastases I reproduce in Figure 394 the appearance of the skull of a patient of ours aged 42, before treat



Fig. 394 Osteolytic metastasis in the skull of a woman, age 42, with carcinoma of the breast

ment and the appearance in Figure 395 after testosterone propionate had been given for 6 months in a dosage of 100 mg three times a week

There have been several recent reports of the results of androgen therapy from clinics where its effects have been specially investigated. Hultberg at the Radium hemmet found that a considerable degree of palliation was obtained in 85 per cent of patients with bone metastases treated with androgen and that they lived appreciably longer than a control series of patients who did not receive androgen Galton reported 20 per cent of substantial remission lasting for more than 6 months in his series of cases of advanced mammary carcinoma treated with androgen

Segaloff and his associates have studied the comparative value of a number of different androgens in advanced cancer of the breast Their findings may be summarized as follows

cil, under the chairmanship of the late Ira T Nathanson, collated the data as to the effects of various steroid hormones in more than 1200 cases of mammary carcinoma A report published by Kennedy and Nathanson in 1953 described in detail the symptoms produced by administering androgens and estrogens The Committee's latest report, published in 1951, embodies a summary of the therapeutic results, as well as recommendations as to the use of hormones These reports should be read by every student of breast carcinoma

Androgen Therapy. The favorable clinical effects of androgen, aside from the relief of pain, are a feeling of well being and a gain in weight The chief unfavorable ones are hoarseness, hirsutism, loss of scalp hair, acne, and the development of a ruddy complexion Kennedy and Nathanson listed these effects and their frequency in tabular form

Table 157 Minimal Incidence of Side-Effects of Testosterone Propionate in Eighty-Two Patients with Advanced Breast Carcinoma
(after Kennedy and Nathanson, 1953)

Side-effects	No of cases analyzed	Incidence %
Hoarseness	77	61
Hirsutism	75	52
Hair loss	55	22
Acne	71	30
Ruddy complexion	64	44
Drowsiness	70	10
Nausea	71	18
Vomiting	70	11
Feeling of well-being	76	76
Weight increase	76	71
Libido increase	59	37
Edema	67	16
Hypercalcemia	73	10
Uremia	72	4

The incidence of these androgen effects increases over a period of months as the treatment is continued The masculinization that the hormone produces in a sensitive feminine woman is sometimes so distressing to her that she finally refuses to continue taking the hormone, even though it has relieved her pain To such a patient the treatment is worse than the disease I am entirely in sympathy with this point of view in these patients, and I have on occasion regretted having given androgen

The masculinization that androgen produces is so unpleasant that this hormone should never be given prophylactically, as Prudente and others have suggested

The Council's Committee in their 1951 report concluded that for soft tissue disease in premenopausal patients, androgen gives the best results, and that it gives the best results for bone metastases at any age The dosage recommended was 150 to 300 mg weekly, given intramuscularly About three months of treatment is required to achieve its full effect Over 50 per cent of patients were im-

Twenty seven patients studied, all either postmenopausal or x ray or surgically castrated

RESULTS

	Number of patients		
	Method of Administration		Total
	Oral	Buccal	
Regression	3	5	8
Unable to evaluate	2	2	4
Progression	5	9	14
Acceleration	—	1	1
	10	17	27

Increasing creatinuria noted in 26 patients, jaundice in 2.

4 *Methylandrostenediol* DOSAGE. 100 mg three times weekly in 22 patients 100 mg daily in 2 patients

RESULTS Objective remissions were noted in 2 patients, i e regression in soft tissue metastases Bony metastases progressed There was no instance of subjective improvement. There was increasing creatinuria There was no effect on the level of urinary gonadotrophic hormone. This preparation was definitely inferior in effect to testosterone

5 *Androstenediol* DOSAGE. 100 mg three times weekly in one group 50 mg daily in other

Twenty-one patients studied

RESULTS. There were no objective signs of regression No subjective improvement was noted There was an increase in urinary 17 ketosteroids and formaldehydogenic hormone No creatinuria or uric acid changes occurred. There was no masculinizing effect

6 *Testosterone propionate*

Type of objective response in 56 patients evaluated

Site	No of cases	Regressive	Progressive
Skeletal	13	38 5/	61 5%
Soft tissue	11	27 3/	72 7%
Both skeletal and soft tissue	21	23 8%/	66 7%

An increase in urinary 17 ketosteroids, prolactin and gonadotrophic hormone occurred in all cases evaluated There was increase in urinary corticoids in patients showing no improvement

Estrogen Therapy The specific side effects of estrogens are less serious than those of androgens but they can be very distressing Nausea and vomiting are common when the hormone is begun but they usually disappear after a few weeks When they are severe the dosage of estrogen should be cut down until a tolerance for the drug is acquired These gastrointestinal symptoms are less frequent with advancing age

The deep pigmentation of the nipple and areola, and the axillary skin which develops when a full estrogen effect is obtained is the most obvious outward sign of it The breasts too often become somewhat engorged

Uterine bleeding is the most troublesome phenomenon produced by estrogen

1 *Androstane-3,17-dione* DOSAGE 100 mg in saline, administered intramuscularly three times weekly

Twenty patients studied—all postmenopausal or surgically castrated

RESULTS This hormone was not as potent as testosterone, dihydrotestosterone or methyltestosterone It was nonvirilizing and caused little or no decrease in urinary gonadotropic hormone



Fig 395 Recalcification of the defects in the skull in the patient shown in Figure 394 as a result of 6 months' treatment with androgen

2 *Dihydrotestosterone* (*androstanolone*) DOSAGE 100 mg in saline, administered intramuscularly three times weekly

Thirty-four patients studied

RESULTS Objective remission was obtained in eight patients An increase in urinary 17-ketosteroids and a decrease in urinary formaldehydogenic hormone and lactogenic hormone occurred in all Virilizing effects were noted in all This preparation was similar in effect to testosterone propionate

3 *Methyltestosterone* DOSAGE Buccal—50 to 100 mg daily Oral—Gradual increase from 300 to 1000 mg daily

Table 159 Results following Treatment with Stilboestrol Dipropionate
(after Douglas, 1952)

Response	No. of cases and ⁄	Av survival months	Av age, years	⁄ premenopausal
Good	33 (10 3)	30 5	66 3	0
Fair	65 (20 2)	19 9	62 9	9 2
None	183 (56 8)	9 1	57 9	17 5
Adverse	33 (10 3)	6 3	54 7	33 3
Withdrawal	8 (2 4)	27 3	58 1	12 5

Segaloff and his associates have made a careful study of the effects of conjugated equine estrogens in 33 patients Five to 10 mg of estrone sulfate was given three times daily Their results were summarized as follows

	Improvement	No improvement	Total
Bone lesions	0	3	3
Soft tissue lesions	11	13	24
Bone and soft tissue lesions	0	6	6
	11	22	33

No improvement was noted in patients below 50 years of age The percentage improving increased with each decade through 80–90 years

Surgical and X-ray Castration for Carcinoma of the Female Breast

The original concept of influencing breast carcinoma by removing the ovaries was conceived by a Glasgow surgeon Mr Beatson more than fifty years ago The fact that ovarian function is related to mammary physiology in both animals and human beings led him to perform oophorectomy on women with cancer of the breast. He obtained striking palliation in a few cases with the operation The procedure was taken up by several English surgeons and during the following decade they did about a hundred of these operations Mr Lett, in 1905 reported that temporary improvement was observed in about one third of the cases As the results of these operations were scrutinized by contemporary surgeons, however the operation lost favor and was generally abandoned

Oophorectomy has been employed sporadically during the last fifty years Isolated reports of its value have occasionally appeared (Raven Horsley) but until recently the operation has not been regularly employed in any institution. Definitive data are still lacking concerning its value Miller and Pendergrass did not find any statistically significant difference in the length of survival of 34 patients whose ovaries had been removed before they developed breast carcinoma The Smiths have recently reported from the Free Hospital for Women however that life was somewhat prolonged in a series of 60 patients in *whom* the ovaries were removed prophylactically Pearson and his associates report their results in a series of 96 patients with metastatic breast carcinoma treated by oophorectomy They claim 44 per cent of objective remissions of the disease for

Since the patients are long past the menopause the bleeding disturbs them It is, however, easily controlled by stopping the estrogen

Kennedy and Nathanson listed estrogen side effects as follows

Table 158 Incidence of Side-Effects of Estrogens Observed in 235 Patients with Advanced Mammary Carcinoma
(after Kennedy and Nathanson, 1953)

Side-effects	No of cases analyzed	Incidence per cent
Anorexia	228	57
Nausea	230	58
Vomiting	223	32
Abdominal distress	209	6
Diarrhea	201	5
Dizziness	189	4
Headache	189	7
Drowsiness	189	8
Libido increase	141	2
Nipple pigmentation	188	80
Areolar pigmentation	185	77
Axillary pigmentation	114	40
Scar pigmentation	68	18
Skin rash	142	1
Itching	143	4
Breast engorgement	178	20
Breast tenderness	179	16
Vaginal bleeding	186	33
Withdrawal bleeding	121	42
Amenorrhea	8	88
Urinary urgency and incontinence	149	28
Edema	193	34
Congestive failure	191	9
Congestive failure (deaths)	191	3
Hypercalcemia		

The Council's Committee in their 1951 report found no essential difference in the effects of four estrogens—diethylstilbestrol, ethinylestradiol, premarin, estradiol dipropionate Given to postmenopausal patients estrogen produced regression of carcinoma involving soft parts in approximately 50 per cent of patients A dose of 15 milligrams of diethylstilbestrol daily was the usual dose A total dose of 4 grams was required to achieve maximal response

While edema and hypercalcemia may develop in any patient with extensive bone metastases, these complications are sometimes precipitated by the administration of estrogen They can be very serious and lead to anuria and death unless recognized and treated promptly The administration of estrogen as a provocative test of estrogen dependence is dangerous and should be condemned

One of the most extensive studies of the value of estrogens that has been reported was that by Douglas She described her results with stilbestrol in 322 patients at Edinburgh as follows

Orchiectomy for Carcinoma of the Male Breast

There is no other method of hormone therapy for any form of cancer which produces palliation as regularly as orchiectomy for carcinoma of the male breast It was Treves who discovered the value of this procedure In 1949 he reported his results in 13 cases of advanced and metastatic carcinoma of the male breast Twelve of these patients were benefited His studies showed that there is a more

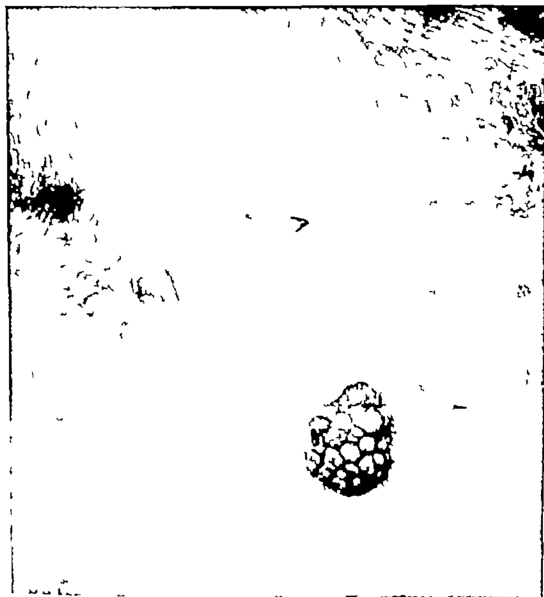


Fig. 396 Advanced carcinoma of the male breast on admission

pronounced effect upon soft tissue disease than upon bone metastasis However both showed regression In his patients treated by orchiectomy average survival time was 31 months as compared with 10 months for those who were not castrated

The effect of orchiectomy upon the primary tumor and regional metastasis in carcinoma of the male breast is illustrated in a patient of ours His history can be summarized as follows

an average period of six and a half months in their premenopausal patients, and 10 per cent of objective remission in their postmenopausal patients

In the 1920's, radiotherapeutists revived the concept of influencing mammary carcinoma by castration, and began to irradiate the ovaries The method has been practiced rather widely with indifferent results Taylor reported that in a series of 47 younger patients with carcinoma of the breast given prophylactic ovarian irradiation there was no demonstrable benefit He concluded, however, that artificial menopause induced by irradiation in patients with inoperable and recurrent carcinoma of the breast had a definite palliative effect in about one-third The most striking benefit was observed in patients with bone metastases Ahlbom was not able to prove that ovarian irradiation given therapeutically to 163 patients with recurrent or metastatic mammary carcinoma had any definite favorable effect Miller and Pendergrass reported their results in 71 patients who had therapeutic ovarian radiation They were not able to show that life was prolonged for these irradiated patients in comparison with patients in their series whose ovaries were not treated Douglas, however, has reported that in a series of 175 patients given ovarian irradiation therapeutically, a good response was obtained in 9 7 per cent and a fair response in 10 9 per cent Most of the patients who were benefited were premenopausal

It is apparent that irradiation given to the ovaries does not suppress estrogen formation entirely in them Evidence to this effect in terms of a smaller rise in urinary gonadotropin, and a smaller decrease in urinary estrogens, following x-radiation of the ovaries as compared with surgical castration, was presented by Nathanson, Rice and Meigs If ovarian function is to be suppressed it is probably better to remove the ovaries surgically

Another type of evidence concerning the relationship of ovarian function to breast carcinoma comes from pathological study of ovaries removed therapeutically from patients with breast cancer and ovaries removed at autopsy of patients dying of breast carcinoma Sommers and Teloh found that a large majority of the ovaries in patients with breast cancer showed hyperplasia of the cortical ovarian stroma, reflecting active secretion of some steroid hormone. They found no difference in the length of life in autopsied patients whose ovaries showed such cortical hyperplasia as compared with the length of life in patients whose ovaries were atrophic Studying the length of life, however, in patients whose ovaries were removed therapeutically, they found that the mean duration of life was 47 months for those with ovarian stroma hyperplasia and only 27 months for those with atrophic ovaries This fact suggested to Sommers and his associates that castration prolongs life in women whose ovaries show stromal hyperplasia

My own point of view regarding oophorectomy is that there is no adequate proof that it is of value when done prophylactically, so I do not recommend it In premenopausal patients who develop recurrence for which irradiation is no longer effective the question of hormonal therapy arises If the problem is the control of pain from bone metastasis androgen is administered If the problem is the control of recurrence in soft tissue I favor oophorectomy combined with adrenalectomy rather than oophorectomy alone, for reasons which will be brought out in a discussion of adrenalectomy

metastasis from breast cancer when estrogen is administered Huggins has shown that adrenalectomy produces palliation after the benefits of orchiectomy have been lost Similarly Luft and Olivecrona report that hypophysectomy has been beneficial after the orchiectomy effect has disappeared

Adrenalectomy

Bilateral total adrenalectomy for advanced disseminated carcinoma was first employed by Huggins and Scott for prostatic cancer patients in 1945 The

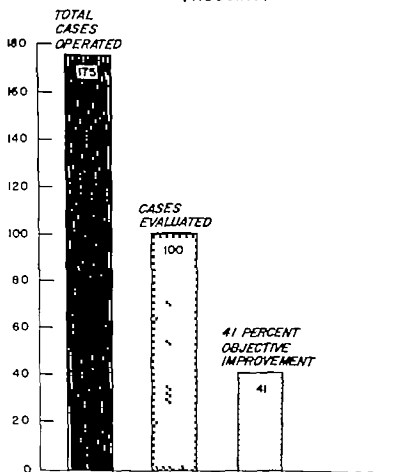


Chart 23

surgical procedure as well as postoperative maintenance of their patients was an heroic effort, because their four early cases were operated upon before the advent of cortisone therapy and with it easy substitution therapy In 1951 Huggins and Bergenstal described bilateral total adrenalectomy for metastatic breast cancer In breast like prostatic carcinoma, the theoretical basis for the operation was the fact of the common embryonic origin of the gonads and adrenal cortex, plus the belief that these are the only structures having the capacity to synthesize endogenous steroid hormonal substances We do not know that the beneficial effects

Mr F A, aged 70, was admitted to the Presbyterian Hospital in October, 1947, with an advanced carcinoma of the right breast The primary tumor formed a protruding mass in the nipple region that measured 3 cm in diameter (Fig 369) There were metastatic nodules in the skin over the anterior pectoral fold, and large fixed axillary nodes There was also a supraclavicular metastasis and a retroperitoneal mass Orchiectomy was performed with remarkable local and general palliative benefits His general health improved strikingly and the breast tumor and its regional metastases regressed remarkably *His appearance 2 years after orchiectomy is shown in* Figure 397 He ultimately succumbed to his disease in May, 1953



Fig 397 The appearance of the local disease in the patient shown in Figure 396 two years after orchiectomy

The mechanism by which orchiectomy affects carcinoma of the male breast is, however, still obscure The theory that orchiectomy depletes the body of androgen and that the carcinoma regresses because it is dependent upon androgen is not an adequate explanation It has been shown that the serum calcium level in these patients with bone metastasis does not increase when testosterone is administered, as the calcium levels are increased in female patients with bone

served a smaller percentage of objective benefit than other investigators no doubt because he is more conservative in his evaluation of the response to the operation

Chart 25 attempts to summarize the results that have been reported to date in the 328 cases of breast carcinoma treated by adrenalectomy

In assessing the place of adrenalectomy in therapy it is worth while to note that, although the surgical Addisonian state of post adrenalectomy patients is relatively easy to manage clinically, it is an undesirable one and not without

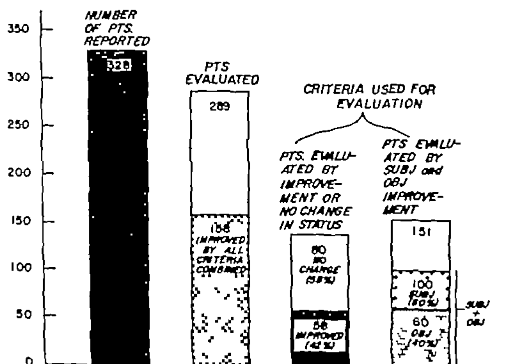


Chart 25

some danger For this reason it will be of interest to observe the results of right adrenalectomy combined with left adreno-splenic venous shunt as described by Galante

A typical example of subjective and objective improvement in advanced mammary cancer achieved by Hudson with adrenalectomy follows.

Mrs. H. S., was 54 years of age at the time of her first admission to the Presbyterian Hospital in 1952. Three years previously she had had a hysterectomy and bilateral oophorectomy She had been followed by her private physician and treated symptomatically for "sciatica since early 1951 At the time of admission in August, 1952, metastatic bone lesions were found in the ribs and vertebrae. Clinical, radiographic, and biochemical search failed to reveal the primary tumor Palpation of the breasts was negative. The patient was treated empirically with testosterone propionate, 100 mg. intramuscularly three times weekly for a period of two years. Some pain relief and slight improvement of some of the bony lesions resulted. She developed hirsutism and was depressed by the masculinization In May 1955 metastatic carcinoma from a

of total adrenalectomy are due to the complete removal of estrogen from the body but the recent work of Huggins and Dao suggests it

The evaluation of the results of adrenalectomy in cancer patients is a difficult and complex problem Subjective improvement in the patient is simple to observe but difficult to measure Objective improvement is almost as difficult to evaluate For example, gain in body weight, and "arrest" of visible and radiographically evident disease are considered "objective" evidence of improvement by some Other workers regard a change from a negative to a positive calcium balance as "objective" evidence of improvement Hudson, who has carried on the studies of adrenalectomy at our Delafield Hospital, has not however regarded any of these evidences as adequate indications of objective improvement These

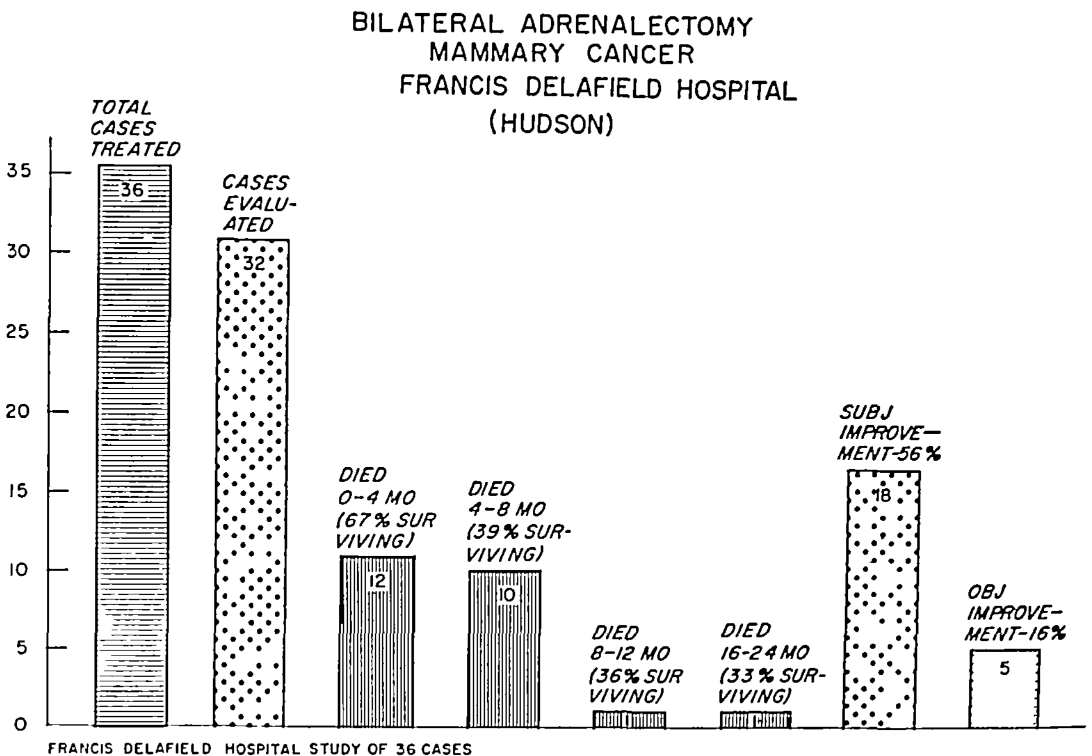


Chart 24

differences as to standards of evaluation undoubtedly contribute to the disagreement in reported results from adrenalectomy

Huggins and his associates at the University of Chicago have now reported their experience with adrenalectomy in 175 breast cancer patients The results obtained in the first 100 patients in his series are shown in Chart 23

Cade has also described his results with adrenalectomy in 69 patients with mammary carcinoma He obtained subjective improvement in 56 per cent of his patients and objective benefit in 35 per cent

Hellström has reported the Karolinska Institute results with adrenalectomy in 51 patients There was immediate improvement in 35 of 51 cases, but prompt relapse in 11 of these He observed improvement for more than six months in 14 patients, and emphasized his inability to select patients who will benefit from the operation

Hudson's results at our Delafield Hospital in 36 patients with mammary cancer who were treated by bilateral adrenalectomy are shown in Chart 24 He has ob-

served a smaller percentage of objective benefit than other investigators no doubt because he is more conservative in his evaluation of the response to the operation

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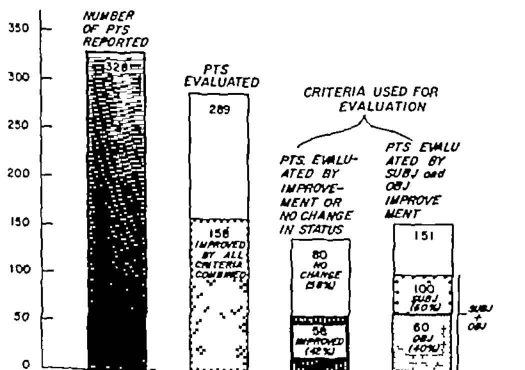


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primary carcinoma of the left breast was established by pathological diagnosis Bone marrow aspirations of the iliac crest also showed carcinoma By this time she had become completely refractory to androgen therapy and had developed extreme pain, restricted use of both lower extremities, and pathological fracture of the left hip

Bilateral total adrenalectomy was performed after Smith-Peterson nailing and plating of the left hip Postoperatively the patient has become pain-free There has been a 30 lb gain in body weight The residual virilizing signs and symptoms from the androgen therapy have almost disappeared Her emotional attitude is cheerful The bony metastases have regressed, disappeared, or healed The osteoblastic metastasis visible in the right hip before adrenalectomy (Fig 398) has disappeared since adrenalectomy (Fig 399) The pathological fracture of the left hip in an area of osteolytic metastasis is well healed six months after adrenalectomy



Fig 398 Pre-adrenalectomy osteoblastic metastasis of right femur



Fig 399 Appearance of right femur six months after adrenalectomy

This patient is an example of both subjective and objective improvement following adrenalectomy for widespread metastatic breast cancer Since her ovaries had been removed in 1949, three years before the recognition of her metastatic mammary carcinoma, it seems logical to attribute the beneficial effects solely to total adrenalectomy

It is important to recognize that there are several limitations to the performance of adrenalectomy Hudson's experience, which agrees in general with that of surgeons elsewhere, indicates that the following categories of patients are unsuitable for treatment by adrenalectomy

(1) Those with hepatic metastasis or insufficiency, as indicated by biochemical evidence preoperatively, or the finding of metastatic lesions at the time of operation

(2) Those with cardiorenal insufficiency

(3) Those with pulmonary insufficiency as indicated by a pronounced reduction in the maximal breathing capacity due to the lymphangitic type of pulmo-

nary metastases Temporary impairment of pulmonary function due to accumulation of pleural effusions is not a contraindication

(4) Those with cerebral metastasis This is a contraindication only in patients who have convulsions

(5) Any patient whose general physical condition would normally preclude major surgery

Hudson believes that we do not yet know enough about the results of adrenalectomy to be able to select the patients who will benefit from it Dao has described the titer of estrogen excreted in urine as one of the most reliable indices for predicting a good response to adrenalectomy He claims 75 per cent of good results following adrenalectomy in patients who had large amounts of estrogen in the urine Hudson s personal experience leads him to reserve judgment on this question

Hypophysectomy

During the last five years both surgical removal and irradiation of the pituitary gland have been used for recurrent breast carcinoma in several clinics Luft and Olivecrona whose studies of this problem are outstanding, have reported their results in 30 patients treated by hypophysectomy Initially Luft reported that all women over 60 years of age and all patients with brain and liver metastasis died immediately after operation Other contraindications to hypophysectomy included cardiac insufficiency and any situation in which increased intracranial pressure had developed In 7 patients there was regression of the local cancerous lesion and in 5 others decrease or disappearance of pulmonary and pleural involvement. In one patient there was a beneficial effect lasting for 28 months postoperatively

Ray has performed hypophysectomy in 51 patients and reports objective improvement including so-called arrest in 26 There seems to be no particular cell type of breast cancer which responds favorably to hypophysectomy As is the case with adrenalectomy the disease has in a few instances responded well to hypophysectomy in both females and males.

In Glasgow Forrest and Brown are attempting to destroy the pituitary with radon implants inserted through the nose. It is not yet known what degree of destruction of the gland can be achieved by this method The evidence that Olivecrona has obtained from his surgical studies indicates that the pituitary must be completely removed if the procedure is to be effective

Both adrenalectomy and hypophysectomy must at present be regarded as experimental procedures, of undetermined value. They produce more subjective than objective benefit There is no question but that the objective benefit in some patients is so dramatic as to seem miraculous but there have not been enough of these miracles to tell us how long the benefit lasts

It is impossible as yet to assess the comparative value of the two procedures Even at the Karolinska Institute in Stockholm where comparative studies of adrenalectomy and hypophysectomy have been carried on for a longer time than anywhere else, no final conclusions regarding their value have been drawn as indicated by a recent statement by Hultberg, as follows

"It is at present quite impossible for me to make an in any way satisfying

comparative study of the results of hypophysectomy and adrenalectomy in mammary cancer We have now about 120 cases with adrenalectomy performed and about 60 cases treated with hypophysectomy and as yet we have not been able to draw any straight lines for the indications for the one or the other of these two procedures "

Both adrenalectomy and hypophysectomy are surgical procedures of considerable magnitude, and their value is at present so questionable that they should not be considered until all other methods have failed Radiotherapy should certainly be tried first for local recurrence or metastasis When it no longer controls the pain produced by bone metastasis, androgen should be given In aged patients the administration of estrogen gives such comparatively good results for all types of recurrence and metastases excepting those in bone, that it should be tried Only after all these methods have failed is it just, in my opinion, to turn to the surgical methods of altering the hormonal status

Summary

Hormonal treatment for mammary carcinoma, which gave such encouraging promise a decade ago, has proved to be a weak crutch upon which we have to rely when surgery and irradiation are no longer of any value The dramatic effects of certain types of hormone therapy such as orchiectomy for carcinoma of the male breast, and the near miracles infrequently observed following adrenalectomy or hypophysectomy, inspire the hope that some day hormonal methods which can be depended upon to give good results in a higher proportion of cases will be found But the indiscriminate use of these operations at present can do a good deal of harm By this statement I do not mean to discourage research in this very important field It must be pursued with determination

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CHAPTER 30

CARCINOMA OF THE MALE BREAST

Carcinoma of the breast occurs so rarely in men that it is not at all well known either to patients or physicians and it is therefore apt to be missed and diagnosed late. When the disease is advanced the results of treatment are very poor Education is needed to the effect that breast cancer occurs in males that it has the same general characteristics as in females and that the surgical attack on it is often successful when the diagnosis is made early

Frequency

The disease is indeed infrequent Treves has recently published his data regarding a total of 146 cases—by far the largest series of cases ever reported In his clinic carcinoma of the male breast constituted about 1 per cent of all primary breast carcinomas in both sexes Williams found a somewhat greater frequency —1 to 88—at St Bartholomew s Hospital In the Presbyterian Hospital only 16 cases of primary carcinoma of the male breast were observed over a 22 year period 1933 to 1955 During this same period more than 2000 primary breast carcinomas occurring in females were seen The relative frequency of the disease in males in our hospital is therefore somewhat less

Age Incidence

Wainwright computed the average age in 325 cases which he collected and found it to be 52.6 years In Treves s series of 146 cases it was 52.1 years. In Huggins and Taylor's series of 75 cases it was 64 years This is a somewhat later age than that at which carcinoma of the breast occurs in women In our Presbyterian Hospital series of cases of carcinoma of the female breast the average age of the patients has been approximately 50 years

From the point of view of differential diagnosis it is important to note that the youngest patient with definite breast carcinoma that Wainwright found was 23 and that Treves s youngest patient was 24 Treves s series includes two other patients in their late twenties, and seven in their thirties It is therefore fair to say that carcinoma is seen only with extraordinary rarity before the age of 30

Etiology

There is a lamentable lack of data as to familial history in the published reports of carcinoma of the male breast Neither Wainwright, Huggins and Taylor or Treves presented any information as to family history of their patients

A family history was recorded in 13 of the 16 patients in our series In 11 there was no record of breast carcinoma But one of the other patients had a maternal aunt who had had the disease, and another had a daughter who developed breast carcinoma at the age of 33

In view of the established familial character of breast carcinoma in the female it is most important to establish the facts concerning this question in the male

It is not infrequent for men with carcinoma of the breast to give a history of antecedent trauma Treves reports that 12 per cent of his patients gave such a history He was unable to trace any definite correlation between trauma and the origin of carcinoma, however

There have been several reports in the German medical literature recently (Gleichmann, Meyer-Laack, Ritschel and Schultze-Jena, Botsztejn and Schinz) which suggest that the increased frequency of gynecomastia in the European countries where starvation conditions existed during the recent war can be correlated with a subsequent increase in carcinoma of the male breast

The question of whether or not carcinoma of the male breast can be induced by the administration of estrogen, as in prostate carcinoma, remains a controversial one I have already discussed it in Chapter 17

Symptoms

Treves's data regarding symptomatology are so much more extensive than any other that I reproduce his table listing the symptoms in his patients

Table 160 Initial Symptom in 146 Cases of Cancer of the Male Breast
(after Treves, 1955)

Symptom	No of cases
Breast mass only	89 (67 4%)
Breast mass plus	
Retracted nipple	7
Discharging nipple .	4
Discharging nipple, pain	1
Encrusted nipple	3
Encrusted nipple, pain	1
Nipple discharge only	8
Nipple encrustation only	5
Nipple retraction only	4
Nipple encrustation, retraction	0
Ulceration	7
Axillary swelling	3
Pain only	0
Pain, breast mass	0
Total	132
Uncertain	14
	146

The evidence suggests that a nipple discharge occurs more frequently with carcinoma of the male breast than with the disease in females Thirteen of Treves's 146 patients had true nipple discharge not associated with ulceration

Williams recorded the presence of a nipple discharge in 6 of his 20 cases but he did not specify whether or not it was associated with ulceration Two of our 16 patients gave a history of a nipple discharge unrelated to ulceration In one the first sign of disease was a slight amount of bloody discharge, which stained his pajamas, occurring seven years previously Examining his breast he found a small mass beneath the nipple which when he pressed it produced the nipple discharge He consulted a physician who told him it was only a pimple The mass persisted and grew very slowly in size The nipple became retracted Six



Fig. 400 Massive mucoid carcinoma of the male breast.

months before admission he noticed a few small nodules around the retracted nipple The breast finally began to pain him and he decided to consult a surgeon

There is no doubt but that men with breast carcinoma come considerably later for treatment than women who develop the disease. The average duration of the breast tumor on admission in Wainwright s series of cases was 2.4 years Every series of cases of carcinoma of the male breast contains a number of cases in which it would appear that the lesion had been present many years In Treves s series 13 per cent of the patients had had their tumor for four years or more One of Huggins and Taylor's patients had had an ulcerated tumor for thirty years

A family history was recorded in 13 of the 16 patients in our series In 11 there was no record of breast carcinoma But one of the other patients had a maternal aunt who had had the disease, and another had a daughter who developed breast carcinoma at the age of 33

In view of the established familial character of breast carcinoma in the female it is most important to establish the facts concerning this question in the male

It is not infrequent for men with carcinoma of the breast to give a history of antecedent trauma Treves reports that 12 per cent of his patients gave such a history He was unable to trace any definite correlation between trauma and the origin of carcinoma, however

There have been several reports in the German medical literature recently (Gleichmann, Meyer-Laack, Ritschel and Schultze-Jena, Botsztejn and Schinz) which suggest that the increased frequency of gynecomastia in the European countries where starvation conditions existed during the recent war can be correlated with a subsequent increase in carcinoma of the male breast

The question of whether or not carcinoma of the male breast can be induced by the administration of estrogen, as in prostate carcinoma, remains a controversial one I have already discussed it in Chapter 17

Symptoms

Treves's data regarding symptomatology are so much more extensive than any other that I reproduce his table listing the symptoms in his patients

Table 160 Initial Symptom in 146 Cases of Cancer of the Male Breast
(after Treves, 1955)

Symptom	No of cases
Breast mass only	89 (67 4%)
Breast mass plus	
Retracted nipple	7
Discharging nipple .	4
Discharging nipple, pain	1
Encrusted nipple	3
Encrusted nipple, pain	1
Nipple discharge only	8
Nipple encrustation only	5
Nipple retraction only	4
Nipple encrustation, retraction	0
Ulceration	7
Axillary swelling	3
Pain only	0
Pain, breast mass	0
Total	132
Uncertain	14
	146

The evidence suggests that a nipple discharge occurs more frequently with carcinoma of the male breast than with the disease in females Thirteen of Treves's 146 patients had true nipple discharge not associated with ulceration

In Huggins and Taylor's series of 50 primary cases 72 per cent had clinical involvement of axillary nodes on admission

A few examples of the Paget's type of carcinoma of the breast have been described (Sarason and Prior Treves)

Differential Diagnosis

Carcinoma of the male breast is a rare disease which has to be distinguished from several much more frequent and entirely harmless lesions which also form tumors in the male breast The most frequent of these is the adolescent type of benign hypertrophy of the breast This occurs with puberty or sometimes a year or so later and forms a discoid mass beneath the areola The youth of the patient and the well delimited character of the tumor and its lack of fixation serve to distinguish it True gynecomastia occurring in the late teens or early twenties is usually apparent from the larger and softer nature of the tumor which mimics the character of the female breast on a small scale Hypertrophy of the male breast due to liver or thyroid disease or of idiopathic origin may form a discoid, movable, somewhat tender tumor beneath the areola Carcinoma of the male breast is so rare before the age of 30 that there is no justification for biopsying tumors in these younger patients Their benign nature is apparent moreover from their physical character

In older patients beyond the age of 50 carcinoma of the breast has to be distinguished from the senile type of benign hypertrophy of the breast I have described this rather frequent but not very well known condition in Chapter 3 This form of hypertrophy has two characteristics which almost always make it possible to distinguish it from carcinoma It begins as a tender small discoid tumor situated beneath the areola Its tenderness is out of all proportion to its size. Small carcinomas are not ordinarily tender More important is the well delimited, rounded movable character of hypertrophy Carcinomas are usually poorly delimited and somewhat fixed I see a good many older patients with the senile type of hypertrophy and I rarely find it necessary to biopsy their lesions In the typical case of hypertrophy the tenderness will begin to diminish after two or three months, and within six months the tumor itself will disappear If it persists much longer or if it is in any way atypical I biopsy it

Pathology

Carcinomas of the male breast show the same microscopical patterns as the disease in the female breast. In fourteen of our sixteen Presbyterian Hospital cases, adequate tissue was available for study The tumors were classified as follows

Papillary carcinoma	1
Circumscribed carcinoma	1
Mucoid carcinoma	1
Intraductal carcinoma	3
No special microscopical type	
Grade I	1
Grade II	2
Grade III	5

Figure 402 shows the papillary carcinoma in our series and Figure 403 the

In our Presbyterian Hospital series of only 16 patients there were two who had apparently had their carcinoma for a very long time, one was the patient whose story I have just mentioned whose history began with a nipple discharge seven years previously The other patient's tumor, as it appeared on admission to the hospital, is shown in Figure 400 It was a massive mucoid carcinoma which had begun as a small tumor beneath the nipple eight years previously, and had grown slowly during the intervening years

One of our 16 Presbyterian Hospital patients did not find his own breast lesion It was discovered by his internist in the course of a routine physical examination

Physical Characteristics

Carcinoma developing in the male breast forms a hard, poorly delimited tumor usually situated beneath the nipple or areola All our patients have had a



Fig 401 The typical appearance of a locally advanced carcinoma of the male breast

tumor Since the carcinoma develops so close to the nipple, changes in it are apparent in many of the patients The nipple was retracted in 7 of our cases, and it was ulcerated in 5 of them As the disease progresses it also narrows the areola, and finally appears on the surface of the areola and the skin immediately surrounding it, in the form of small nodules Figure 401 shows the typical appearance of the disease at this stage

These carcinomas of the male breast are often fixed to the underlying pectoral fascia, since they lie very close to it

Extensive metastases to axillary lymph nodes are often present on admission.

In Huggins and Taylor s series of 50 primary cases 72 per cent had clinical involvement of axillary nodes on admission

A few examples of the Paget s type of carcinoma of the breast have been described (Sarason and Prior Treves)

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No special microscopical type	
Grade I	1
Grade II	2
Grade III	5

Figure 402 shows the papillary carcinoma in our series, and Figure 403 the

Fig 402 Papillary carcinoma of the male breast



Fig 403 The circumscribed type of carcinoma of the male breast

circumscribed carcinoma One of our well differentiated intraductal carcinomas is shown in Figure 404

If the four special types of carcinoma which are represented in our small series of tumors are counted as well differentiated as indeed they should be, 7 out of 14 or one half of our carcinomas were well differentiated This is a much higher proportion of well differentiated carcinomas than is to be expected in a series of mammary carcinomas in the female I assume that the occurrence of so many well differentiated carcinomas in our small Presbyterian Hospital series is fortuitous.



Fig. 404 Intraductal carcinoma of the male breast.

Treatment

Carcinoma of the male breast has the reputation of being exceptionally difficult to cure I believe this is because the disease is so often far advanced when it is first diagnosed Treves classified only 69 per cent of his patients as having operable disease Sixty two per cent of Huggins and Taylor's patients were operable Nine of our 16 patients were operable according to our criteria.

It is generally agreed that the preferable treatment is radical mastectomy Treves reports a 29 1 per cent five year absolute survival rate for the 120 cases in his series admitted between 1924 and 1949 Eighty-one of these 120 patients were classified as operable Thirty four or 44 per cent, (of those apparently treated by radical mastectomy) survived five years. In Huggins and Taylor s series of cases 5 of the 25 who were treated by radical mastectomy were still well after 5 years

In our smaller Presbyterian Hospital series of cases five patients, whose disease was in an operable stage, were treated by radical mastectomy more than five years ago Three of them are alive and well All three had well differentiated intraductal carcinoma One had axillary metastases The other two did not

Treves did not correlate the histological grade of the carcinomas in his series with the cure rate beyond pointing out that all six of his patients with the papillary type of carcinoma were cured Huggins and Taylor failed to describe the microscopical types of the carcinomas in their series of cases

This fragmentary evidence suggests that the microscopical type of carcinoma in the male breast may be the most important factor in determining prognosis

From the technical point of view radical mastectomy for carcinoma of the male breast is no different from the operation as it is performed for the disease in the female, with one exception I refer to the absolute necessity for skin grafting in the male In the male such a broad area of skin and underlying tissues should always be sacrificed that a defect measuring from 15 to 20 cm remains on the chest This cannot be covered without skin grafting

I have not referred here to the hormonal treatment of inoperable and recurrent carcinoma of the male breast, since I have already discussed it in Chapter 29

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CHAPTER 31

THE PROBLEM OF BREAST CARCINOMA IN PROFILE

The challenge to society which the problem of breast carcinoma presents prompts a brief review of our knowledge concerning the disease at the midpoint of the 20th century

Within the last 100 years which include virtually the entire span of what constitutes modern medical knowledge, much has been learned regarding breast carcinoma. Experimental work with mice who get the disease very much as human beings do has succeeded in finding but not in characterizing, an ultramicroscopic particle which induces the disease This particle resembles some viruses in size and in certain other characteristics This field of research gives promise of some day identifying the cause of breast cancer in mice If this is achieved it may help to explain the etiology of the disease in human beings.

Modern clinical methods have assembled a great deal of knowledge concerning the occurrence the diagnosis, the natural history and the treatment of breast carcinoma Society does not use this knowledge very efficiently however There is a great need of education of both laymen and physicians

We know that in most western countries breast carcinoma is the most frequent of all cancers being indeed about twice as frequent as any other type The disease is surprisingly infrequent, however in societies where marriage is early children numerous and breast feeding customary This fact suggests that the development of carcinoma in the mammary glands may be related to their function that is to nursing We have, however very few specific data as to the frequency of carcinoma in nursed breasts in comparison with breasts that have never functioned The custom of breast feeding is disappearing so rapidly in western countries that unless an intensive study of the question of its relationship to breast carcinoma is made very soon the control data from women who have nursed will no longer be available The Scandinavian countries are virtually the only ones in which such a study could be made today The public health agencies in these countries, however lack funds for such an investigation I can think of no better use for the funds for the study of cancer raised by public subscription in our country Our modern society which expends great sums of money for a great variety of luxuries, should be able to afford an inquiry such as this which may lead us to at least a partial understanding of the cause of breast cancer

We have at present no indication of any other practical way of reducing the

frequency of breast cancer We know that the disease is about four times as frequent in women who develop grossly evident breast cysts or who have a family history of breast carcinoma, but the only thing that can be done in a practical way for women in these two categories is to attempt to make certain that their breast carcinomas will be detected early if and when they do develop

Early detection is the next important step toward the control of breast cancer Its early recognition can contribute much more to improve the chance of cure than any possible refinement of treatment Neither the women who develop the disease nor the physicians to whom they come for help are succeeding as well as they might in detecting and diagnosing it early Women discover breast tumors by accident, instead of by systematic search, and therefore sometimes only after the tumor has been present a long time It is perfectly possible however, to train them to examine their own breasts at regular intervals and to be comparatively expert at breast examination The motion picture film which I made for this purpose in cooperation with the American Cancer Society has had some success, and is the kind of educational effort that should be extended

The two groups of women which I have mentioned who are more likely to develop breast carcinoma should be examined by a physician every three months, if they do not succeed in learning how to examine their own breasts

To achieve this plan for detecting breast carcinoma an elaborate educational effort will be required Education of laymen regarding cancer is a two-edged sword, however, and will do more harm than good if it frightens them We know beyond question that it is fear more than ignorance that makes women with a breast tumor delay so long in consulting a physician The average duration of symptoms continues to be from 7 to 10 months The challenge to educators is to shorten this period of delay by dispelling fear

When the patient with breast carcinoma finally consults her physician, he misses the diagnosis in about 25 per cent and causes further delay This is a distressing fact for medical educators to face, and necessitates improvement in clinical teaching regarding breast cancer

There is as yet no good evidence that society is succeeding in meeting this educational challenge, either as regards lay or professional education We must hope that progress will be made, and must use the great skill and energy which our present day publicists possess, and which they so often devote to causes less urgent than the detection and diagnosis of cancer

We need to look soberly at what the results of the modern treatment of breast carcinoma really are if we are to be convinced of the need for improving them Table 161 shows the absolute survival rates for breast carcinoma for those institutions from which data have been published from which absolute rates can be computed The 5 year survival rate from most clinics is approximately 40 per cent and the 10 year rate approximately 25 per cent

How can these results be improved? The first step must be the adoption of a policy of careful selection of patients for operation in place of the indiscriminate use of operation which now prevails, at least in our country The use of specific criteria of operability such as I have described in Chapter 26, will exclude from operation many of the patients who cannot be cured by the Halsted radical

mastectomy This kind of selection will not only avoid a great number of futile and harmful operations, but it will at once result in a marked improvement in the relative cure rate Surgeons will be inspired by these improved results to perform the operation more thoroughly and more carefully and their improved technique will produce superior results which will elevate the over all survival rates

Table 161 Absolute Survival Rates from Various Hospitals

Years covered by study	Author and year of publication	Hospital	Total no of primary cases	Absolute 5 year survival rate	*Absolute 10-year survival rate
1936–1941	Nohrman 1949	Radiumhemmet Stockholm	1042	40 1	23 4
1937–1944	Smithers 1952	Royal Cancer Hospital London	1093	34 6	20 7
1936–1942	Windeyer 1949	Middlesex Hospital London	917	34 0	20 7
1931–1944	Nielsen 1951	Copenhagen Radium Centre	1405	38	18
1930–1939	Williams et al. 1953	St Bartho o new's Hospital London	1044	34 0	20 0
1936–1947	Bryant et al. 1954	University of Michigan Hosp Ann Arbor Mich	742	40 2	
1935–1942	Haagensen and Stout 1948	Presbyterian Hospital, N Y	668	47 9	33 4
1941–1947	McWhirter 1955	Royal Infirmary Edinburgh	1882	42 0	25 0

* Number of survivals expressed as a percentage of the total number of primary cases.

The results of the Halsted radical mastectomy when it is performed upon properly selected patients, are better than is generally realized For example in a personal series of ward and private patients selected for operation on the basis of our *clinical* criteria of operability the five year clinical cure rate was 56 7 per cent and the five year survival rate 66 6 per cent In a subgroup of patients in this series, in *whom there were no clinically involved axillary nodes and in whom none of our five grave signs of locally advanced carcinoma were present* the 5 year clinical cure rate was 74 6 per cent and the 5 year survival rate was 84.5 per cent. Yet in 34 per cent of the patients included in this subgroup *microscopical study*

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When the patient with breast carcinoma finally consults her physician, he misses the diagnosis in about 25 per cent and causes further delay This is a distressing fact for medical educators to face, and necessitates improvement in clinical teaching regarding breast cancer

There is as yet no good evidence that society is succeeding in meeting this educational challenge, either as regards lay or professional education We must hope that progress will be made, and must use the great skill and energy which our present day publicists possess, and which they so often devote to causes less urgent than the detection and diagnosis of cancer

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How can these results be improved? The first step must be the adoption of a policy of careful selection of patients for operation in place of the indiscriminate use of operation which now prevails at least in our country The use of specific criteria of operability such as I have described in Chapter 26, will exclude from operation many of the patients who cannot be cured by the Halsted radical

the efforts of research workers surgeons radiotherapeutists pathologists and educators—all cooperating to make the best use of the weapons which modern science has given us The courage which our patients display should inspire us to put aside prejudice and in all humility to unite in a common effort to conquer the disease

showed metastasis in either one or two nodes I wish to emphasize again that I attribute these results to critical selection of the patients for operation rather than to any technical facility The radiotherapeutists have not presented proof that they can obtain results with primary irradiation treatment, in similarly selected series of cases of breast carcinoma, which approach this surgical achievement These facts indicate that at present we have no form of treatment for the disease as successful as the Halsted radical mastectomy performed in critically selected cases This should encourage those surgeons who are disheartened with their results and who are at the moment tempted to surrender the treatment of all patients with breast carcinoma to the radiotherapeutists

The important recent development in our knowledge of the natural history of breast carcinoma is the discovery of the frequency of occult metastases in the internal mammary and supraclavicular lymph nodes In patients whose disease has been regarded as operable in most clinics, internal mammary metastases are found in approximately 30 per cent and supraclavicular metastases in about 10 per cent In our clinic we have developed biopsy methods of detecting the presence of these metastases in the regional lymph node filter We have used the presence of these metastases as *biopsy* criteria contraindicating operation The application of these new and more strict criteria has reduced our operability rate to approximately 50 per cent

The therapeutic problem which the presence of these internal mammary and supraclavicular metastases presents has not been solved The conventional radical mastectomy does not, of course, attempt to remove these nodes Various new surgical techniques for extended operations designed to remove them have not yet proved their value Radiotherapy has not yet been shown to have more than a temporary growth restraint upon metastases in these lymph nodes, but it has the advantage of a lesser capacity to do harm than overextended surgery

With the limitation of the use of surgery which critical evaluation of the extent of breast carcinoma, both locally and in the regional lymph node filter, implies, the role of radiotherapy in the attack upon the disease becomes increasingly important Irradiation is today just as important as surgery, if not in terms of the number of patients it cures, at least in terms of the number of patients whose disease is palliated In terms of the prerogatives that organized medicine and society have given them American radiotherapeutists are not as well prepared as their European colleagues to meet this responsibility Their training has unfortunately not been separated from that of x-ray diagnosticians in most American hospitals and is as a result, to a degree, inferior They have not, in most hospitals, been given the clinical services and beds which they need for the evolution of their specialty They do not have, except in a very few institutions, the higher voltage equipment which we believe is advantageous All these limitations handicap the radiotherapeutists, whose specialty should be recognized as one of the most demanding in modern medicine At the moment they are engaged in protracting and further fractionating their irradiation Clinical evidence suggests that this will add to its efficacy But it is a task requiring exceptional patience and exactitude

If we are to make real advances in the control of cancer of the breast we need

the efforts of research workers, surgeons radiotherapeutists, pathologists and educators—all cooperating to make the best use of the weapons which modern science has given us The courage which our patients display should inspire us to put aside prejudice and in all humility to unite in a common effort to conquer the disease.

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